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ENURESIS

A GENETIC STUDY

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MINNEAPOLIS

Probably every physician who has treated enuretic children has observed that more than one case of enuresis frequently occurs in a single family. The tendency has been, however, to explain the familial incidence on an environmental basis. The theory that the condition is a conduct disorder has recently been supported by Hamill [1] and Beverly.[2] From observations made at the University of Minnesota it seems probable that the occurrence of enuresis [3] in a child is determined primarily by a hereditary factor and only secondarily by environmental or emotional causes. The purpose of this paper is to present data supporting this thesis.

Information has been collected for 59 clans, including 221 fraternities, in which, of a total of 787 individual members, 239 are known to have been enuretic. In order to secure adequate data for this study, the parents of the child representatives of each clan have repeatedly been interviewed at the clinic in connection with the treatment of the child. By letters and personal visits to the homes, where contacts have been made with grandmothers and great-aunts, it has been possible to augment the original information given at the clinic and at times to add other limbs to the family trees. Physicians and nurses who are members of the clans have been consulted and have always been cooperative in replying to requests for information. No cases have been included in which the enuresis could reasonably be attributed to a congenital anomaly, a mental defect, a known endocrine disturbance or associated pyuria or nephritis. Since, according to the White House Conference Reports,[4] 95.4 per cent of children are trained for bladder control by

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Clinical material for this study has been obtained chiefly in the pediatric outpatient department of the University Hospital, of which Dr. C. A. Stewart, Associate Professor of Pediatrics, is in charge. In considering the genetic significance of the collected data, I have conferred with Dr. C. P. Oliver, Assistant Professor of Zoology.

1. Hamill, R. C.: Enuresis, J. A. M. A. **93**:254 (July 27) 1929.
2. Beverly, B. I.: Incontinence in Children, J. Pediat. **2**:718 (June) 1933.
3. Whenever the word enuresis is used, nocturnal enuresis is to be understood.
4. White House Conference on Child Health and Protection, Committee IIIB: Education and Training of the Infant and Preschool Child, New York, D. Appleton-Century Company, 1933.

the age of 3 years, this age was arbitrarily chosen as that at which bed-wetting normally ceases. Therefore, in the data used for statistical purposes (tables 1, 3, 4, 5 and 6), all persons under 3 years of age have been excluded, but they are represented in the family trees by double concentric squares or circles. The information obtained regarding the families of the 221 fraternities mentioned meets these requirements, and these sibships have been made the basis of the following study. The hypothesis is proposed that enuresis is determined by a single recessive gene substitution.

Before undertaking an analysis of the data relative to enuresis, it seems desirable to present the definitions given by Guyer [5] and Hogben [6] for the following genetic terms which, for the sake of clearness, will be used in this discussion. A dominant character is a character from one parent which manifests itself in the offspring to the exclusion of a contrasted character from the other parent. A recessive character is a character from one parent which remains undeveloped in the offspring when it is associated with the corresponding dominant character from the other parent. A determiner is the distinctive cause or unit in a germ cell which determines the development of a particular character in the person derived from that cell. The terms gene and factor are used as synonyms of determiner. Siblings (sibs) are members of the same fraternity (brothers or sisters) irrespective of sex. In pure breeds in which the determiners are alike, the individual is said to be a homozygote with reference to that character, while in breeds in which determiners are unlike, the individual is termed a heterozygote with reference to the character. Or, to use the adjective forms, a pure black guinea-pig is homozygous for pigmentation, and an albino guinea-pig is homozygous for whiteness, while a cross between the two is a heterozygous for pigmentation.

In table 1, the 221 families concerning which there is adequate information are arranged in three groups according to whether both parents are affected (i. e., there is a history of enuresis), one parent is affected or both parents are normal. Groups II and III are further divided into two subgroups: (*a*) families in which 1 or more offspring are affected and (*b*) families in which none are affected. It will be seen that in the 2 families of group I (table 1), in which both parents have had enuresis, all 6 children have had enuresis. In group II_a, in which 1 parent is known to have been enuretic, there are 38 families with a

5. Guyer, M. F.: Being Well-Born, Indianapolis, Bobbs-Merrill Company, 1927.

6. Hogben, Lancelot: Genetic Principles in Medicine and Social Science, London, Williams and Norgate, Ltd., 1931.

total membership of 132. Of these, 70 persons (or 53 per cent) have been enuretic. In group III_a, in which both parents are normal, 163 cases of enuresis have occurred (roughly, 36 per cent) in 112 families with a total of 447 members. In groups II_b and III_b, as stated earlier, there are no enuretic siblings.

It is in group III_a, in which both parents are normal and 1 or more children enuretic, that justification is found for the choice of the term recessive with reference to enuresis, since, if the trait were dominant, the 2 normal parents of each family of this group would have to be homozygous normal persons (as the quality does not manifest itself in them) and hence could not transmit to offspring a factor which neither of them carried. The 163 affected offspring of group III_a can therefore be explained only on the assumption that enuresis is a recessive character,

TABLE 1.—*Distribution of Enuretic Persons in the 221 Families of the 59 Clans Studied*

Group	Parents	Subgroup	Number of Matings	Total Siblings	Number Affected	Percentage Affected
I	Both affected.....	..	2	6	6	100
II*	One affected.....	a	38	132	70	53
		b	7	15	0	0
III*	Both normal.....	a	112	447	163	36
		b	62	187	0	0
Totals.....			221	787	239	

* This group is divided into two subgroups: (a) families in which 1 or more offspring are affected and (b) those in which no offspring are affected.

in which case all of the normal parents of these offspring must be heterozygotes (i. e., carriers of the trait). Detailed discussion of the theoretical and observed percentages of affected persons in group III_a, with the genetic significance of those values, will be found beginning on page 5.

In table 2, which presents the theoretical scheme of inheritance according to the mendelian law, black indicates the recessive quality (in this case, enuresis), and white, the dominant quality (in this case, normalcy). A black cross indicates a carrier. Squares represent males, and circles, females. Three types of persons must be considered: (1) the recessive (enuretic) person, who is a homozygote with reference to enuresis, (2) the dominant (normal) person, who is homozygous for the normal character, and (3) the hybrid person, who is heterozygous for the character difference. Since the normal condition is dominant, the heterozygote will be normal but will carry the enuretic character recessively and may therefore be referred to as a carrier. Six types of matings are then possible, and the offspring (or siblings) in each case will follow the scheme of inheritance shown in table 2 with reference to enuresis. It will be noted that recessive (enuretic) offspring will

occur only in types A, B and D of this table, in which both parents carry the gene, either as homozygotes or as heterozygotes. In type A, in which both parents are recessive (enuretic), all of the offspring will be recessive (enuretic); in type B, in which 1 parent is recessive (enuretic), half of the offspring will be recessive (enuretic), and half will be dominant (heterozygous normal) types, while in type D, in which both parents are dominant (normal persons but carriers), 25 per cent will be recessive (enuretic), and 75 per cent dominant (i. e., 25 per cent will be pure normal persons and 50 per cent will be carriers).

If one compares tables 1 and 2, it is apparent that group I (table 1) is in agreement with the scheme of inheritance as set forth for type A

TABLE 2.—*A Theoretical Scheme of Inheritance According to the Mendelian Law, Showing Six Types of Matings with Their Offspring* *

Type	Parents †		Offspring	
A ‡	Both recessive	■ x ●	100%	recessive ■ (●)
B §	One recessive One heterozygous	■ x ⊗	50% 50%	recessive ■ (●) heterozygous ⊠ (⊗)
C	One recessive One dominant	■ x ○	100%	heterozygous ⊠ (⊗)
D ‖	Both heterozygous	⊠ x ⊗	25% 25% 50%	recessive ■ (●) dominant □ (○) heterozygous ⊠ (⊗)
E	One heterozygous One dominant	⊠ x ○	50% 50%	heterozygous ⊠ (⊗) dominant □ (○)
F	Both dominant	□ x ○	100%	dominant □ (○)

* The symbols employed here are fully explained in the text.
† The sex may be reversed.
‡ This is the prototype of group I, table 1.
§ This is the prototype of group IIa, table 1.
‖ This is the prototype of group IIIa, table 1.

of table 2. The 2 pairs of affected parents have transmitted the factor determining enuresis to 100 per cent of their offspring. The group, however, is too small to exclude accident in the selection of cases. In group II_a (table 1), the actual value of 53 per cent enuretic offspring is slightly in excess of the theoretical value of 50 per cent for its prototype B of table 2. It is impossible to determine whether the matings of group II_b, by which there were produced 15 normal offspring, correspond to type B or to type C of table 2, since the 1 normal parent in each case may be a heterozygote (type B) or a homozygote (type C) and cannot be identified except by the grandchildren of later generations. The 15 normal offspring observed in group II_b may likewise be heterozygous or homozygous, and some heterozygous siblings from this group may then account for the 3 per cent discrepancy in group II_a.

Group III_a (table 1), with an actual value of 36 per cent for affected offspring, shows an 11 per cent excess as compared with its prototype D of table 2, which has a theoretical value of 25 per cent. The statistical explanation of this discrepancy will be given later in a quotation from Hogben, and the observed 36 per cent, corrected according to a biometric formula, will be shown to correspond to the expected value of 25 per cent. Members of group III_b (table 1) may be identified with the offspring of types E or F of table 2, or with the 75 per cent dominant siblings (normal persons and carriers combined) of type D. In the last case, the law of chance has operated so that these carrier parents have produced no affected offspring, just as it has determined in group III_a that other carrier parents have had 11 per cent more affected offspring than are to be expected theoretically.

TABLE 3.—*Distribution of Enuretic Members According to the Size of the Fraternity When Both Parents are Heterozygous* *

s	n_s	r_s	$s.n_s$	q^s	$1-q^s$	$\frac{s.n_s}{1-q^s}$	Corrected p
1	13	13	13	0.7500	0.2500	52.0	0.25
2	19	26	38	0.5625	0.4375	86.8	0.299
3	25	39	75	0.421875	0.5781	129.7	0.300
4	20	27	80	0.316406	0.6836	117.0	0.231
5	8	13	40	0.237304	0.7627	52.4	0.248
6	13	20	78	0.177978	0.8220	94.9	0.211
7	2	2	14	0.133484	0.8665	16.2	0.123
8	5	9	40	0.100113	0.8999	44.4	0.203
9	3	6	27	0.075085	0.9249	29.2	0.205
10	2	3	20	0.056313	0.9437	21.9	0.137
11	2	5	22	0.042236	0.9578	23.0	0.217
Totals.....		163	..	.....	.....	667.5	

* The probability (p) that the offspring will be affected is theoretically 25 per cent. The corrected value of p is derived from the formula:

$$p = \frac{\Sigma r_s}{\Sigma \frac{s.n_s}{1-q^s}} \times 100,$$

in which s represents the size of the fraternity; n_s, the number of fraternities of size s; r_s, the number of affected members, and q, 0.75.
The corrected value for p equals 24.44 ± 1.16 per cent.

After pointing out that any quantitative study of an inherited character must consider chiefly the large group of families with heterozygous parents, i. e., group III_a of table 1 or its prototype D of table 2, Hogben [7] said:

The simplest approach to the problem is as follows: If the trait appears in such a family and is determined by a recessive gene, we know that both parents must be heterozygotes. Where more than one gene is involved, the familial incidence of the defect will be too low to provide any suspicion of its genetic basis. If human families were large, it would only be necessary to take a census of normal and affected individuals in all families containing the latter. The proportion of affected individuals would then be ¼. Since human families are

7. Hogben,[6] p. 51.

very small, many heterozygous parents will have no affected offspring. Statistically these will be compensated by other families in which the proportion of affected is in excess of expectation. The latter will be included in our census. The former will not. Thus there will be three families of single children without the recessive trait for every family of one recessive who is a single child. Clearly, if all families containing recessives are taken from the human population, the ratio of the total number of recessives to the total number of individuals in such a group of families will be greatly in excess of the theoretical proportion of recessives in all families of two heterozygous parents.

Since it is impossible in the human race to identify a carrier who does not have recessive offspring, Hogben,[6] following Lenz, employed a biometric formula to make allowances for the discrepancy that arises by sampling. If p represent the probability that the offspring of two

TABLE 4.—*Data Arranged for Comparing the Observed Number of Recessive Members (t_s) with the Expected Number (r_s)* *

s	n_s	c_s	k_s	$n_s k_s$	t_s	r_s	Δ	σ
1	13	4.0000			13	13.00		
2	19	4.5714	0.12245	2.3266	26	21.71	4.29	1.53
3	25	5.1892	0.26297	6.5742	39	32.43	6.57	2.56
4	20	5.8514	0.42005	8.4010	27	29.26	3.26	2.89
5	8	6.5557	0.59178	4.7342	13	13.11	0.11	2.18
6	13	7.2991	0.77595	10.0874	20	23.72	3.72	3.29
7	2	8.0783	0.97024	1.9405	2	4.04	2.04	1.39
8	5	8.8900	1.1724	5.8620	9	11.11	2.11	2.42
9	3	9.7306	1.3802	4.1406	6	7.30	1.30	2.04
10	2	10.5970	1.5917	3.1834	3	5.30	2.30	1.78
11	2	11.4850	1.8053	3.6106	5	5.74	0.74	1.90
Totals.....				50.8605	163	166.72		

* This is calculated according to the formula:

$$\Sigma r_s = \Sigma n_s p c_s \pm \sqrt{\Sigma n_s k_s},$$

in which the probable percentage of recessive members (p) equals 25, c_s and k_s are varying constants; Δ represents the difference between t_s and r_s and the standard deviation (σ), is $\sqrt{n_s k_s}$.

In this table

Σt_s equals 163, and Σr_s equals 166.72 ± 7.13.

heterozygous parents will be recessive (theoretically, 25 per cent) and q, the probability that the offspring will be normal (75 per cent), $p + q = 1$. If s represents the number of offspring in the family; n_s, the number of families having s offspring, and r_s, the number of recessive offspring in n_s families,

$$p = 100 \frac{\Sigma r_s}{\Sigma \frac{s.n_s}{1 - q^s}} = 25 \text{ per cent}$$

"If this condition is satisfied," according to Hogben, "we may infer that a familial trait is determined by a single recessive gene substitution."

The data from group III_a are arranged according to Hogben's scheme in table 3. Dividing the summation of r_s by the summation of $\frac{s.n_s}{1-q^s}$, the corrected value of $p = 100 \times \frac{163}{667.5} = 24.44$ per cent. The standard

deviation is 1.16 per cent.[8] There is, accordingly, satisfactory correspondence between the theoretical value for p, i.e., 25 per cent, and the observed value of 36 per cent, as corrected by Hogben's formula to 24.44 ± 1.16 per cent. Therefore, the assumption is warranted that enuresis is a hereditary trait determined by a single recessive gene.

Using the same values for the constants c_s and k_s as he used in determining the standard deviation of p,[9] Hogben developed a second formula[10] for calculating the expected number of recessive persons from data derived from small families with the computation for standard deviation for that number:

$$\Sigma r_s = \Sigma n_s \, pc_s \pm \sqrt{\Sigma n_s k_s}$$

In this formula r_s represents the expected number of recessive persons; n_s, the number of s-membered fraternities (as before), and p, the probable percentage of recessive persons (25); c_s and k_s are varying constants read from a table. The observed value (Σt_s) is then compared directly with the expected value (Σr_s), and their difference (Δ) is compared with the standard deviation (σ) of the expected value. Table 4 shows the data arranged for application of this formula. By this method

$$\Sigma t_s = 163, \text{ and}$$
$$\Sigma r_s = 166.72,$$

and the difference between Σt_s and Σr_s is 3.72, which is less than the standard deviation, 7.13. The table has been arranged so that the difference (Δ) between the observed number of recessive persons in each group (t_s) and the expected number (r_s) can easily be compared with the standard deviation (σ). It will be seen that for fraternities of 5 members, the correspondence between t_s and r_s is close. In sibships of less than 4 members, the observed value (t_s) is greater than the expected value (r_s), while in those of more than 4 members, the expected value is greater. This is in accord with the law of chance as pointed out by Hogben. The discrepancies in the group balance each other in the total figure given earlier. The application of the second formula confirms the finding that enuresis is a hereditary trait determined by a single recessive gene.

In discussing the problem of enuresis, investigators have frequently pointed out that there is a relative and absolute predominance of males among those affected. It will be seen that this is true in my group (table 5). The reason for this difference is not clear at present. There

8. The standard deviation is derived according to Hogben's formula, $\sigma = \sqrt{\frac{\Sigma n_s k_s}{\Sigma n_s c_s}}$, in which c_s and k_s are varying constants (J. Genetics **25**:111 [Nov.] 1931). The values of these constants are listed in table 4.

9. Hogben, Lancelot: Genetic Analysis of Familial Traits: Single Gene Substitutions, J. Genetics **25**:97 (Nov.) 1931.

10. Hogben, Lancelot: Factorial Analysis of Small Families with Parents of Undetermined Genotype, J. Genetics **26**:75 (July) 1932.

is no evidence that enuresis is a sex-linked character. The figures presented by the White House Conference, Committee IIIB (table 135 [4]), show a slight tendency on the part of girls to establish bladder control at an earlier age than do boys. Also, in an unpublished series of observations,[11] fewer instances of bed-wetting were reported for girls than for boys on the night preceding the interview. My data regarding the sex of normal and enuretic persons in the fraternities studied are arranged in table 5.[12] According to the Chi-square test for a fourfold table, the Chi-square is 3.97; hence p equals 0.046. Such a value for p means that the aforementioned difference between the sexes may occur by chance in 5 of 100 samples. This is a level at which it is logical to assume that the difference between sexes with reference to enuresis is significant. As this sample may be one of the 5 unusual ones, application of the Chi-square test to further data is desirable in order to prove or disprove the predominance of enuresis in males.

TABLE 5.—*Showing Distribution of Normal and Enuretic Persons According to Sex*

	Boys	Girls	Totals
Normal	161	161	322
Enuretic	128	90	218
Totals	289	251	540

The Chi-square value equals 3.97, and the probability (p) 0.046. This signifies that there are five chances in a hundred for a difference such as that which exists between these two groups to arise by sampling.

As to the accuracy of the data presented here, it is a foregone conclusion that no human genetic history of this character can be perfect. Every effort has been made in this study to confirm the information given. For 81 per cent of the enuretic persons there are exact data as to the approximate age of the person and as to how long the enuresis continued (table 6). In most instances, the informants have given undeniable evidence that their report was correct, the child having lived or visited in the informant's home. Positive data from parents and grandmothers have been considered authentic. In the case of siblings reported to be normal, there is a greater chance for error, since not all people can give or wish to give information of such a personal character. Whenever there was doubt about the normality of an individual member,

11. Personal communication from Dr. John E. Anderson, chairman of Committee IIIB, White House Conference on Child Health and Protection.

12. In a few instances, data as to the sex of the siblings in the earlier generations were not recorded at the time of the original interview, and it has not been possible to secure this information. These families have therefore been omitted from table 5.

his fraternity was not included in the aforementioned tables. It should be emphasized that this information cannot be secured in a single interview, and that one must win the confidence of the informant before reliable data can be hoped for.

DESCRIPTION OF FAMILY TREES

A few family trees are given to illustrate how enuresis appears in one generation after another. As already explained, a square indicates a male member, and a circle, a female member; when the sex is not known, a diamond is used. Black indicates the recessive character (in this instance, enuresis) and white the dominant character (here, normalcy); when there is authentic information that the person was normal, a dot has been placed in the center of the circle or square. Children under 3 years of age, as well as those who died in infancy, are designated by double concentric circles or squares. A black cross has been used to indicate a carrier. In most instances the cross marks a person who must be a carrier if the trait is recessive, i.e., one who had recessive offspring or who had 1 recessive parent; in a few cases it has been used to give the more plausible interpretation as to the passage of the trait (through a carrier) down to affected persons. Members of the clan referred to in the text may be identified by the numbers enclosed in parentheses, which correspond to those above the squares and circles representing the persons in the charts. Patients are indicated by stars; informants are indicated by arrows. The age to which the enuresis continued is noted below the square or circle which designates the person.

Fraternity 18 (chart 1) is interesting because the parents (*14, 15*) are recessive. There are persons on both sides of the family who have had a severe type of enuresis persisting into adult life (*9, 12, 14, 18*). The father (*14*) and 2 of his brothers (*9, 12*) were enuretic. They had 3 normal siblings, 2 of whom (*10, 11*) have married and have 3 normal children (*19, 20, 21*); their other children are still under 3 years of age. The paternal grandparents (*3, 4*) are too old to give any reliable information. The mother's (*15*) enuresis continued till she was 8 years old. She had an enuretic brother (*17*) and a normal sister (*16*). Her parents and their siblings are all dead except a maternal aunt (*7*). This aunt has been interviewed and recalls definitely that the daughter (*18*) of a cousin (*8*) was persistently enuretic at the age of 17 or 18. No other persons are known to have been affected. One would suspect that there were at least 2 carriers (*1, 2*) in the great-grandfather's family, and that the grandmother (*6*) and her cousin (*8*) transmitted enuresis to their offspring (*15, 17, 18*). There are now 4 members of fraternity 18, a girl (*25*) having been born since this study was begun. The 2 older children, a boy, now 13 (*22*), and

a girl, aged 5 (*23*), have been observed since September 1932. When they were first seen, they were wetting the bed every night. For two months they were kept on a low fluid intake; then for financial reasons it became impossible for the mother to follow any diet strictly. In spite of free soup and milk at school, with a shortage of food at home, the mother cooperated intelligently in restricting fluids. By December 1932 the boy was waking himself and his sister every night, and both beds were dry except on three occasions, when the girl was not wakened.

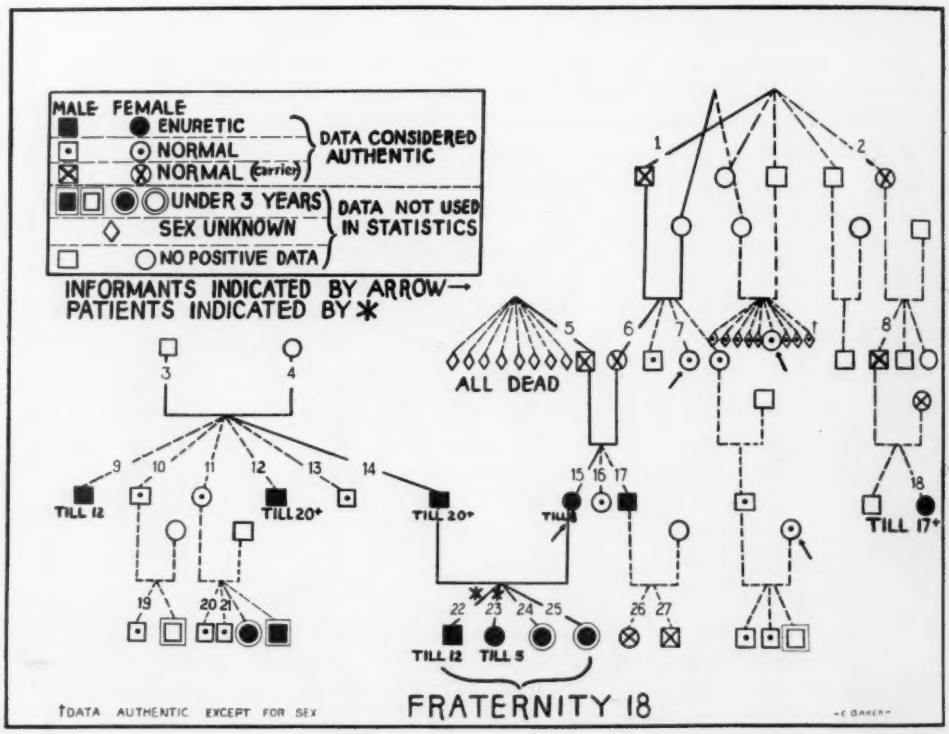

Chart 1.—Pedigree of fraternity 18.

Neither child had any trouble during the spring and summer of 1933, but in the fall the boy again had two "wet" nights. The mother followed a similar regimen with the third child (*24*), who is 2 years old; the child now has a wet bed about once a month.

The pedigree of fraternity 6 was obtained with some difficulty by the paternal aunt (*8*) of the patient (*37*), the mother (*15*) having died a year or so before. Following the mother's death, the 4 children (*36, 37, 38, 39*) were placed in the homes of different relatives. It will be seen that all 4 have a history of enuresis. According to the aunt's history, the mother, by intuition or diligence, or by both, was able to control the children's enuresis quite well. With the change of environ-

ment after her death, however, the 3 younger children frequently wet the bed; the oldest, now 12 years of age, has had a dry bed since he was 8. This family affords a good example of the way in which hereditary and environmental influences interact to determine the age at which the enuretic child establishes control.

When the 10 year old boy (*37*) came to the clinic in October 1932, he was frequently wet day and night. He was placed on a special diet with a total fluid intake of 900 cc. and given extra rest. Enuresis occurred only five times up to the middle of April. The diet was then made less strict, as the boy was waking himself at night. In October 1933 he was again brought to the clinic because he was wetting the bed every night. With restriction of water, control was reestablished.

TABLE 6.—*Maximum Age at Which Enuresis Is Known to Have Occurred*

Age	Male	Female
3	6	9
4	6	10
5	6	6
6	10	6
7	9	9
8	11	5
9	7	4
10	12	6
11	6	5
12	16	13
13	3	2
14	9	1
15	1	1
16	5	2
17	1	1
18	1	0
Over 20	4	1
Totals	113	81

It will be seen from the family tree that of 8 members of the father's family, the father (*14*) and an uncle (*9*) were affected, while another uncle (*7*) was a carrier, as shown by his 3 affected offspring (*23, 24, 25*). One would seem warranted in concluding that the affected uncle (*9*) mated with a homozygous normal person (*20*), since their 4 children (*30, 31, 32, 33*) were normal. This view is further supported by the fact that enuresis did not occur in the siblings (*18, 19*) or in their offspring (*26, 27, 28, 29*). Neither paternal grandparent (*2, 5*) was affected, but the grandfather had a brother (*3*) whose enuresis persisted until he was 13 years of age. A brother (*4*) of the grandmother (*5*) married a sister (*1*) of the grandfather (*2*), and one of their 3 children (*6*) was affected, showing that 2 siblings of each paternal grandfraternity (*1, 2, 4, 5*) must have been carriers. It was not until October 1933 that the aunt learned through the maternal grandmother that the patient's mother (*15*), as well as her only sister (*16*), had had

enuresis. The grandmother does not recall at what age the children's mother (*15*) established control but said that both of her daughters were slow in this respect, the aunt (*16*) presenting a greater problem as a baby than the mother (*15*). At 9 years of age, the children's mother had a long period of enuresis. There is no record of urinalysis; the condition was associated with tonsillitis, and a tonsillectomy was performed. One would wish to know whether a urinary infection was present as a factor in causing this recurrence of bed-wetting.

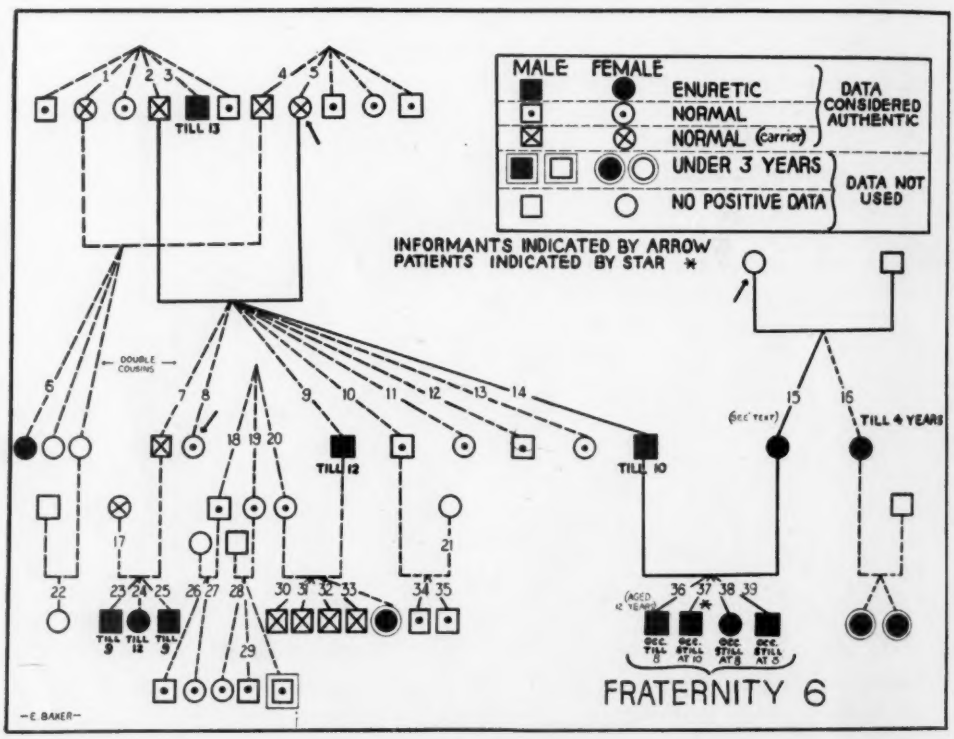

Chart 2.—Pedigree of fraternity 6.

In fraternity 7 (chart 3) the patient (*14*) is a boy, aged 12, who came to the dispensary for treatment at the age of 11, at which time he was wetting the bed about three times a week. When last seen, he had had a wet bed only once in six months and did not have a recurrence with the onset of cold weather. His only sister (*15*) was trained at 9 months of age. The mother (*5*) was a bed-wetter until 12 years of age. The maternal grandparents (*1, 2*) do not know of any instances of enuresis among their siblings. The grandmother, however, was not brought up in her parents' home, so that she cannot state the age at which her younger brothers were trained. So far as she knows, they were normal. It must be that one brother (*3*) was a carrier, as he

had 2 affected offspring (*8, 9*), who are cousins of my patient's mother (*5*). The siblings of the mother (*5*) are all normal, but a brother (*6*) must be considered to be a carrier, since of his 4 children, although 3 were trained at 1 year, the oldest (*16*) wet the bed until she was 5 years old. A sister (*7*) of the mother married an enuretic person (*10*), but owing to the fact that she is a homozygous normal person, or by chance, her 6 year old son (*17*) is normal. It is interesting to note that her husband's sister (*11*), who also was enuretic, theo-

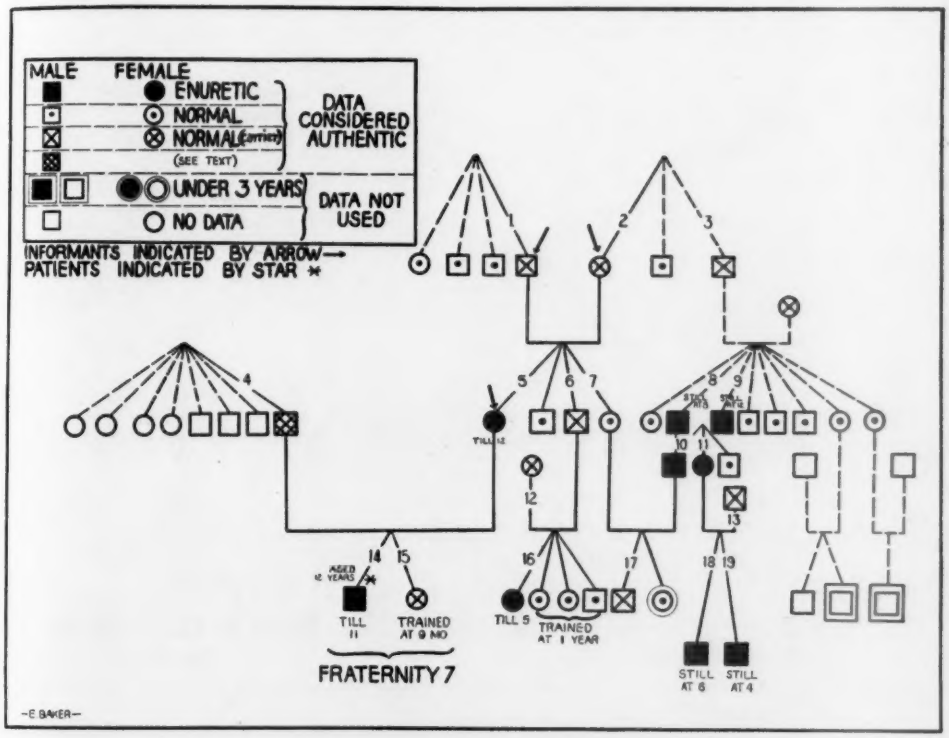

Chart 3.—Pedigree of fraternity 7.

retically had a less fortunate mating (with a carrier [*13*]), as both of her children (*18, 19*) are affected. The father (*4*) of our patient came to America at the age of 16 and cannot give any information about his family. He does not recall having had enuresis previous to his arrival in this country, but remembers definitely that for three months after coming here he lived in a hotel in New York and wet the bed every night. The enuresis (?) stopped as abruptly as it began. A urinalysis was not made at the time. Should the father be included as a recessive person or as a carrier? Because of the extenuating circumstances, he has not been classed as recessive. It is evident that he

is a carrier of the gene, since the trait appears in his son. If he were recessive, the 1 normal child (*15*) could not be explained by the mendelian law.

In fraternity 51 (chart 4) there is an excellent example of type B. The father (*24*) of my patients (*35, 36*) is enuretic, and the mother (*30*) must be a carrier. The 2 older children (*35, 36*), boys of 10 and 8 years of age, respectively, are typically enuretic, while the younger child (*37*), now 3 years old, has had a dry bed for almost a year. The

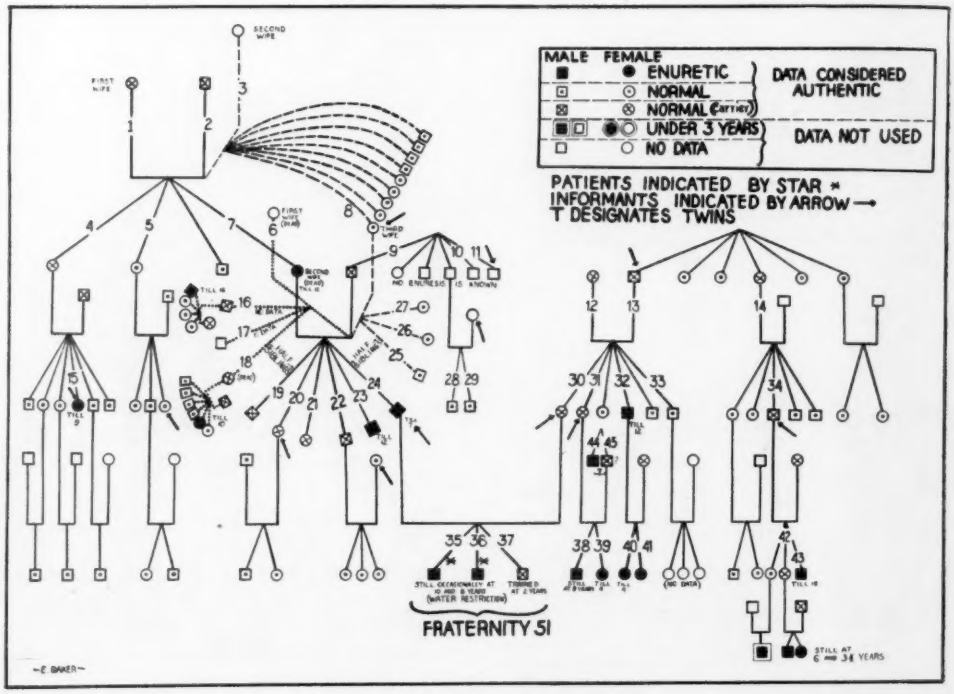

Chart 4.—Pedigree of fraternity 51.

father's family is also of type B; the grandmother (*7*) was enuretic until adolescence, and the grandfather (*9*) is evidently a carrier. Of the 6 siblings, 2 are recessive (*23, 24*) and 4, normal (*19, 20, 21, 22*). The latter, according to the mendelian law, should be carriers. Two did not marry, and 2 (*20, 22*) have presumably (though not necessarily) mated with normal persons, as 1 (*20*) has 2 and the other (*22*) 3 normal children. Any enuretic offspring appearing later will demonstrate that both parents were carriers. Returning to the great-grandfather (*2*), the informant (*8*) told of 13 offspring, 4 by his first wife, my patients' great-grandmother (*1*), and 9 by a second wife (*3*). It will be seen that the first wife (*1*), like her husband, must have carried the gene,

but that the children's grandmother (*7*) was the only affected sibling. Another daughter by this first marriage (*4*), however, was a carrier, transmitting the trait to one of her daughters (*15*). This girl's enuresis continued until the age of 9, according to her story; her parents explained this by saying that she was not robust like her brothers and sisters, none of whom wet the bed. A second sister (*5*) of my patients' grandmother is reported as normal and having 3 normal children and 2 normal grandchildren. The great-grandfather's second wife (*3*) pre-

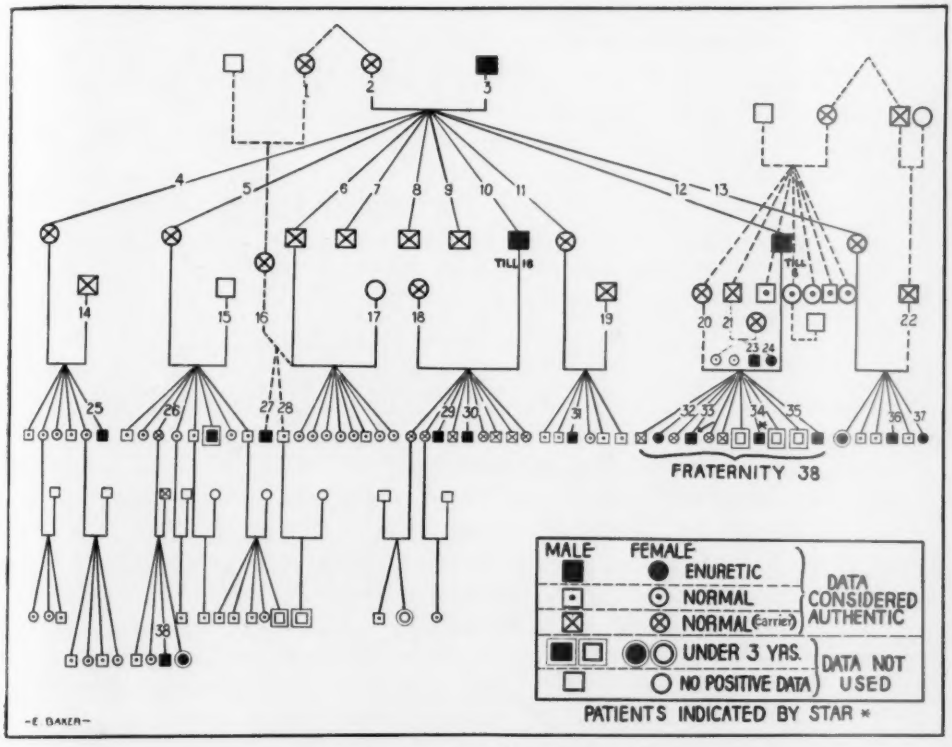

Chart 5.—Pedigree of fraternity 38.

sumably was normal, since my informant (*8*), who is 1 of her children, is sure there was no instance of bed-wetting in the sibship of 9 members.

Turning to the grandfather (*9*), the data become exceedingly valuable from a genetic standpoint. As will be noted by the chart, he married three times and must have been a carrier. There is no record as to his first wife (*6*) and no positive record regarding her 3 offspring (*16, 17, 18*), as they were considerably older than the rest of the family. Presumably (but not necessarily) she was a homozygous normal person. Her son (*16*) must have inherited the factor, since his wife (also a

carrier of the trait) bore him 1 enuretic son as well as 3 normal daughters. There are authentic data on these children, the boy's enuresis having continued until he was about 16. A daughter (*18*) of the first wife also carried the gene to 1 of her 6 offspring. The grandfather's second wife was the recessive grandmother (*7*) of my patients, and, as already noted, 2 of her 6 children (*23, 24*) were enuretic. The third wife (*8*), my informant for this section of the pedigree, is a half-sister of the second wife and 1 of the 9 normal offspring by the great-grandfather's second marriage. Her 3 children (*25, 26, 27*) are normal, and none have married. In the grandfather's (*9*) fraternity of 6 members, 3 different informants have assured me that they know of no enuresis. None of these informants is especially qualified to give reliable data on this particular sibship; all of the siblings except the youngest brother are dead. Only 1 of the siblings (*10*) has had children. His 2 sons (*28, 29*) are normal.

The mother (*30*) of fraternity 51 did not have enuresis but is proved to be a carrier by her 2 enuretic offspring. Her sibship is of type D (both parents [*12, 13*] are heterozygous). One of her brothers (*32*) was enuretic until 12 years of age. He must have married a carrier, since both of their offspring are affected (*40, 41*). One sister (*31*), a carrier, is mated to a carrier (*45*), as shown by their 2 enuretic children (*38, 39*). This father (*45*) is 1 of similar male twins, but data are insufficient to indicate whether they are a monozygotic or a dizygotic pair. They were separated at an early age because of the death of their parents. Twin *45* does not remember about himself, but has a vivid recollection of the punishment inflicted by an aunt on twin *44* at the age of 4 years because he wet the bed while visiting at her home. He can fix the exact date because it was coincident with the birth of a baby sister. It would be dangerous to draw any conclusions without further data, but this bit of information is suggestive when one notes the black square and circle which designate the only offspring of *31* and *45*. Positive data regarding the 3 daughters of the youngest brother (*33*) are lacking. So far as the informants know, the daughters are normal. Tracing the pedigree back one generation further, there are authentic data to the effect that there was no enuresis in the maternal grandfather's (*13*) family. One of his sisters (*14*), like himself, must have been a carrier, having transmitted the defect through a son (*34*) to a grandson (*43*) and through a granddaughter (*42*) to 2 great-grandchildren.

As already noted, my patients (*35, 36*) are typically enuretic. The older brother (*35*) was made the subject of an intensive two month study in water metabolism by Dr. Irvine McQuarrie at the University Hospital; a report will be made later. I have repeatedly observed the

difficulty which the nurses have experienced in rousing him for the collection of specimens. During waking hours, however, he is exceptionally cooperative. The 8 year old boy (*36*) was studied at the dispensary and during a short stay in the hospital. The youngest child, also a boy (*37*), presents no problem, as he was trained soon after he was 2 years old. Theoretically he is a carrier.

The pedigree of fraternity 38 (chart 5) has been arranged to show all of the descendants of a homozygous recessive person (*3*) who married a heterozygous normal person (*2*). In the second generation there were 10 children, of whom 2 were recessive (*10, 12*) and eight were normal. According to the mendelian law, all of the normal offspring should be heterozygous for enuresis, i. e., carriers of the trait. Three of the 8 normal persons have not married; 4 (*4, 6, 11, 13*) have proved themselves to be carriers by transmitting enuresis to 1 or more of their offspring; the fifth (*5*) had 7 normal children (the eighth died in infancy), but 1 of her grandchildren (*38*) was a bed-wetter. The supposition is that the 4 who had recessive offspring, and hence are proved carriers, mated with carriers, while the fifth (*5*) married a homozygous normal person. That at least 1 of her children was a heterozygote is demonstrated by the recessive grandchild (*38*). Three younger children of 5 are still single, and it is probable that there will be more recessive offspring in the third generation as the members of the second generation (the children of *5*) produce more progeny.[13]

The offspring of the third child (*6*) of the grandparents (*2, 3*) present an excellent example of the law of inheritance. By his first wife (*16*) he had 2 sons (*27, 28*), 1 of whom (*27*) was recessive. As will be seen from the chart, he and this wife were cousins, so that the probability is strong that the factor would be transmitted by both parents to the offspring. The "fifty-fifty" average actually shown, although it may be due to chance, is a logical corollary. By a second wife (*17*) there were 8 normal children, which suggests strongly that she was a homozygous normal person. Among the children of a carrier mother (*13*), there is also a high percentage of recessive persons, 2 (*36, 37*) of 5 children having been affected. That there is more than a chance explanation for this is evident when one notes by the family tree that a brother and sister (*12* and *13*) of clan 38 married their cousins (*20* and *22*). That the determiner for enuresis was present in the clan of these cousins is evident if one considers the siblings of 20. Her brother (*21*) has 2 normal and 2 enuretic offspring (*23, 24*).

13. In so prolific a clan it has been impossible to present all of the members of the third and fourth generation graphically, without disregarding age sequence. In this family the three single persons are actually the younger members, although two of them appear earlier in sequence.

It is not surprising to find that 4 of the 8 children of *20* and *12*, who himself is recessive, are recessive; this accords with the mendelian scheme of inheritance (table 2). Among the offspring of the other of the 2 recessive siblings of the second generation (*10*), only 2 (*29, 30*) of 9 have had enuresis.

In the case of fraternity 57 (chart 6) in which both parents are normal, the patients are similar twin girls 13 years of age (*31, 32*). They had a severe type of enuresis and were wetting the bed practically every night when admitted to the clinic at 12 years of age. The enuresis

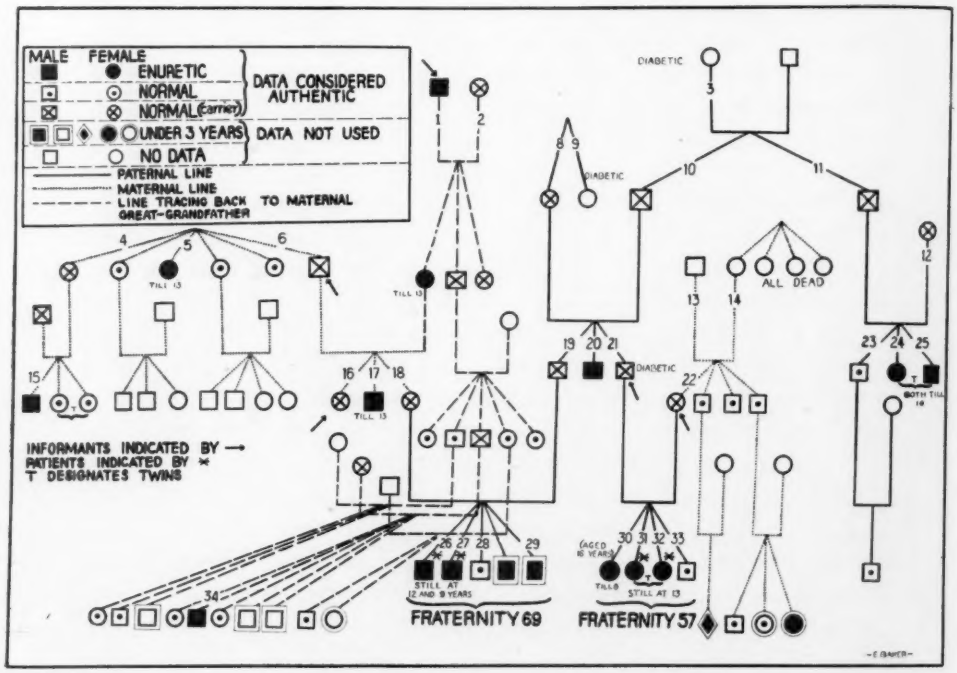

Chart 6.—Pedigree of fraternities 57 and 69.

was controlled by the restriction of fluids, but the bed is still occasionally wet. The question as to whether or not they are monozygotic twins will be discussed later. There are 2 siblings, a sister (*30*), now 16, who was also enuretic until her eighth year, and a younger brother (*33*), who was trained at an early age. The father (*21*) of the 4 children is diabetic, as was also his mother's sister (*9*) and his father's mother (*3*). A test for sugar tolerance gave a normal curve for each twin. The father has 2 brothers (*19, 20*), 1 of whom (*20*) was enuretic until 16 years of age. The other brother (*19*) is the father of fraternity 69. There are no data on the grandparents (parents of *19, 20, 21*), but a

brother (*11*) of the grandfather (*10*) is known to have had twin offspring, male and female (*24, 25*), who were bed-wetters until they were about 16 years of age. The mother of fraternity 57 (*22*) can give no positive information about her relatives. She knows that there was no enuresis among her 3 brothers.

In fraternity 69 (chart 6), the 2 oldest boys (*26, 27*) aged 12 and 9 years, respectively, were wetting the bed almost every night when first seen in July 1933. The third child (*28*) is normal; the fourth died in infancy, and the youngest (*29*) is congenitally defective mentally. An accurate history of their mother's (*18*) family has been secured through an aunt (*16*). An uncle (*17*) had enuresis until he was 13 years old. The maternal grandmother (*7*) and the great-grandfather (*1*) also were affected, the great-grandfather being the informant. That the grandfather (*6*) was a carrier is evident from the enuretic son (*17*). Consistent with this is the finding that he had 1 enuretic sister (*5*) and at least 1 sister (*4*) who was a carrier, who has transmitted the defect to a son (*15*) but not to a pair of twins. A second cousin (*34*) of my patients, on the mother's side, also wets the bed.

The interest in fraternities 57 and 69 centers about the pair of similar like-sexed twins, both of whom are still enuretic at 13 years of age. If monozygotic, the twins confirm in a significant way the thesis that enuresis is a hereditary character. Although one may not establish monozygosity with absolute certainty, not only are there no significant differences to indicate that the pair are dizygotic, but the evidence in favor of their being from a single ovum is unusually strong. There is a striking similarity in appearance and actions, and the twins have always been considered identical by friends and relatives. Twin 31 is left-handed; twin 32 is right-handed. The blood of both falls in group 3 (Moss classification). Roentgenograms made by Dr. Leo Rigler showed identical skeletal development in the 2 children. An examination of the twins by Mr. E. S. T. Lund, of the Department of Education, revealed practically identical body measurements and identical finger-prints and palm-prints and pigmentation of the iris. The reports of Dr. Rigler and Mr. Lund follow.

A comparison of the roentgen films of the twins was made. There was some delay in the ossification in the shoulder, as the epiphysis for the acromion process was just appearing. The process showed distinct irregularity, which was rather unusual and which was almost exactly similar in the 2 twins. The roentgenograms of the wrist and hand showed an exactly similar development even to the extent that only three sesamoids were present. The films of the elbow showed an extraordinary appearance; the epiphysis for the lower end of the humerus was almost completely united, but there was a small, disklike shadow, apparently a portion of the epiphysis for the trochlea, which was not united. This was an unusual appearance, and it was almost exactly similar in the 2 twins. The epiphyses of the feet were exactly similar, even to the extent of the appearance of

the epiphysis for the tuberosity of the fifth metatarsal bone. In the hip joints an os acetabuli was present. This was somewhat uncommon and was present in both girls. The other development around the hip was similar. The entire appearance suggested strongly that the twins are identical.

The twins satisfied in every detail the Stocks criteria for monozygosity, e. g.:

1. When compared digit for digit, homolaterally, eight of the finger-prints were practically identical. The finger-print formulation is given in the following tabulation:

	Right Hand	Left Hand
Twin *31*	Lu Lu Lu Lu_1 Lu	W_2 Wc_3 Lu Lu Lu
Twin *32*	Lu Lu Lu Lu_1 Lu	Lu_2 W_3 Lu Lu Lu

(The subscript numerals indicate the fingers which showed a difference between the twins.[14])

2. The differences in the various bodily dimensions used are as follows:

	Difference Between Twins *31* and *32*, Cm.	Limiting Difference, Cm.
Height	0.5	8.5
Length of head	0.15	0.55
Breadth of head	0.2	0.45
Circumference of head	0.2	1.3
Interpupillary distance	0.1	0.3

The figures in the right-hand column indicate the limiting difference for a diagnosis of like-sexed twins as given by Stocks.[15] It will be noted that the values are well within the limiting difference.

Palm-prints were taken of the mother, the siblings and the twins. The formulations of the palm-prints of the twins were almost identical, although they were decidedly different from those of the 2 siblings. The formulation for the twins was as follows:[16]

	Right Hand	Left Hand
Twin *31*	11-5″.x/9.7.5-0-A^r.0.0.1.V	11-5″.x.7.5-t′-L^r.0.0.V.V.
Twin *32*	11-5″. 9.7.5-0-A^r.0.0.1.V.	11-5″.9.7.5-t′-L^r.0.0.1.V.

The hue and chroma of the irises were seemingly identical in the outer and inner zones, although they differed from those of the siblings and the mother.

Both twins have clockwise hair whorls located in the same part of the occiput.

The blood of the twins falls into group 3 (Moss).

Terman-Binet and Kuhlmann-Binet tests were given by the same examiner. By the Terman test, twin *31* was given an intelligence quotient of 119, and twin *32*, a quotient of 106. By the Kuhlmann test, the rating for twin *31* was 106, and that for twin *32* was 110. The examiner concluded that the girls were about equal in ability, although they did not always do equally well on the same question.

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14. Newman, H. H.: The Finger Prints of Twins, J. Genetics **23**:415 (Dec.) 1930.

15. Stocks, Percy, and Karn, M. N.: A Biometric Investigation of Twins and Their Brothers and Sisters, Ann. Eugenics **4**:49, 1930, table 37.

16. Cummins, Harold; Keith, H. H., et al.: Revised Methods of Interpreting and Formulating Palmar Dermatoglyphics, Am. J. Phys. Anthropol. **12**:415 (Jan.-March) 1929. Newman, H. H.: Palmar Dermatoglyphics of Twins, Am. J. Phys. Anthropol. **14**:331 (July) 1930.

In arithmetical problems of the Terman test, as well as in the interpretation of fables and abstract words, twin *31* excelled, but she failed on other questions which twin *32* answered easily. The examiner noted that the method of attack as well as the phrasing of their answers was alike on most problems. The twins have the same teachers and take the same subjects, but are in different groups of students. That the variation in mental age between the girls is well within the usual limits for a monozygotic pair is shown by a comparison with the data on mental testing of twins which has been collected by Stocks.[17] He derived a correlation coefficient of 0.85 for monozygotic twins, as compared with 0.65 for fraternal twins and 0.45 for siblings.

ENVIRONMENTAL AND EMOTIONAL FACTORS

It has been demonstrated in the preceding pages that enuresis is determined by a single recessive gene substitution. I believe that this hereditary factor—the nature of which has not yet been ascertained—is the primary cause of delayed development of bladder control in children who are commonly termed bed-wetters. One should not, however, ignore environmental factors. Undoubtedly, in milder cases the age at which the enuretic child establishes bladder control is determined by his environment. In severe cases, on the other hand, enuresis apparently runs its course regardless of training. It is in such cases that restriction of the total fluid intake with consequent reduction of urinary output proves especially helpful. Whether by this method one actually hastens the establishment of control or merely furnishes a crutch is an open question. The fact that most of the enuretic children who are cured by restriction of water voluntarily continue to restrict their fluid intake after a more liberal amount of water is allowed is an argument for the second explanation. The frequency with which the disorder recurs in patients who fail to cooperate in this respect strengthens the argument. Certainly every effort should be made, by whatever treatment seems best, to offset the sense of inadequacy which comes to the person who wets the bed.

The handicapped child, no matter what his handicap—clubfoot, a cleft palate, a crooked spine, a speech defect or enuresis—is peculiarly subject to environmental influences leading to emotional conflicts. This does not mean that the environment is necessarily the inciting cause of the enuresis; obviously a habit may become established and may continue after the causative factor has been controlled.

If, as data indicate, enuresis is primarily a hereditary rather than an acquired character (i. e., a conduct disorder for which the parent and the child are responsible), the physician's problem takes on a new aspect, although the details of treatment may be essentially unchanged. The intelligent mother will accept the challenge of a handicap which

17. Stocks, Percy, and Karn, M. N.: A Biometric Investigation of Twins and Their Brothers and Sisters, Ann. Eugenics **5**:24, 1933.

may be controlled with a degree of patience and open-mindedness which she would not assume in dealing with "carelessness" or "naughtiness." The child himself receives a new impetus to control the enuresis when he is made to understand that it is not entirely his fault, and that he must try hard if he is to have a dry bed. Certainly there is as yet no specific cure for enuresis, nor can one hope to predict with any certainty the response of the individual child to the type of treatment instituted until the causative factor is clearly defined.

SUMMARY

1. The pedigrees of 59 clans in which there occur 1 or more enuretic children have been studied, and a hereditary tendency was observed.

2. The hypothesis is proposed that enuresis is a hereditary trait determined by a single recessive gene substitution.

3. Biometric formulas have been applied to data for 112 fraternities with normal parents but including 1 or more enuretic siblings. When the expected percentage of enuretic persons is 25, the observed value corrected by a biometric formula is 24.44 ± 1.16. When the observed number of enuretic persons in these families is 163, the expected number, according to biometric formula, is 166.72 ± 7.13. The hypothesis, therefore, is warranted.

4. Six family trees are presented to illustrate the application of the mendelian law of inheritance to enuresis.

5. A severe type of enuresis is reported in a pair of twin girls of 13 years, whose structural development is shown by roentgen studies to be identical and who satisfy in every detail the Stocks criteria for monozygosity.

6. Environmental influences, especially the attitude and intelligence of the parents, are secondary but important factors, which may alter the course of the disorder.

LIPOID NEPHROSIS

A CLINICAL AND PATHOLOGIC STUDY BASED ON FIFTEEN YEARS' OBSERVATION WITH SPECIAL REFERENCE TO PROGNOSIS

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In the last ten years a tremendous amount of literature on lipoid nephrosis has been published. Since 1918 we have been carefully observing and following up children with lipoid nephrosis. Our first observations were published in 1922 [1] and 1929.[2] It is not our intention to give an exhaustive treatise on the subject in this paper. Recently, Leiter [3] reviewed extensively the subject of lipoid nephrosis both in children and in adults. In this communication we wish to consider certain aspects of this condition, the significance of which can be understood only by the study of patients who have been under continuous observation for a prolonged period. Our primary purpose is to consider the prognosis. Secondarily, the final diagnosis will be considered because it is our impression that in certain cases only after prolonged observation or necropsy can a positive diagnosis be established. A typical case is characterized chiefly by: an insidious onset; frequent remissions of edema; the presence in the urine of large amounts of albumin with a few formed elements; normal blood urea, high blood cholesterol and low serum protein values, and normal blood pressure.

ORGANIZATION AND PROCEDURE

The pediatric department of the Mount Sinai Hospital has a well organized follow-up clinic. After discharge from the hospital each patient is seen as often as it is thought necessary. If a child fails to report at the clinic, a social worker visits the home and urges the parents to bring the child to the clinic. The attendance at the clinic has been excellent. All of the necessary clinical and laboratory examinations are

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From the Pediatric Department and the Laboratories of Mount Sinai Hospital.

1. Schwarz, H., and Kohn, J. L.: Studies of Nephritis in Children: I. Nephrosis, Am. J. Dis. Child. **24**:125 (Aug.) 1922.

2. Schwarz, H., and Kohn, J. L.: Bacteremia and Skin Manifestations in Lipoid Nephrosis, Am. J. Dis. Child. **38**:762 (Oct.) 1929.

3. Leiter, L.: Nephrosis, Medicine **10**:135 (May) 1931.

made, but no treatment is advised or given. If the patient is under the care of a physician, the findings are reported to him.

MATERIAL

This communication consists of a report on thirty-six children who were considered by us at some time to have true lipoid nephrosis. There were additional typical cases which are not included, because they could not be followed long enough to insure a correct diagnosis. The youngest child when first seen was 1½ years old and the oldest, 12. Eighteen, or one half of the children, were under 4 years. There were twenty-three boys and thirteen girls, one of whom was colored. In the literature we find reports of several cases of lipoid nephrosis in children under 1 year (Saldún,[4] Leenhardt, Chaptal, Dufoix and Monnier [5]).

We have grouped our patients as follows: (1) the nine children who were followed to complete recovery; (2) the seven children who when last seen were clinically well but still had albumin in the urine; (3) the two children who had varying degrees of edema when last seen; (4) the eighteen children whose cases terminated fatally (we were able to obtain postmortem examinations in nine instances).

PATIENTS WHO RECOVERED

Nine children seem to have recovered completely. Our criteria of recovery are: freedom from edema, normal urine and normal blood chemistry for at least a year. One child was observed for two years after the onset of symptoms, and one, for over three years; three children were observed for over four years, and four, from eight to ten years. The age of the child at the onset of the illness was not a factor in recovery. Eight of these children were aged 6 years or under (table 1).

Clinically these patients could be divided into two groups: those having symptoms of comparatively short duration and those with symptoms of long duration. The cases could also be arbitrarily classified as being clinically mild or severe. By short duration we mean that the clinical symptoms of nephrosis disappeared after from three to eight months. There were four such cases. These children, however, continued to have urinary albumin for from one to five years. They followed the usual clinical course; three of them were fortunate enough to escape any severe intercurrent infection. They could usually be

4. Saldún, M. L.: Néphrose lipoïdique chez un enfant de onze mois, Arch. de méd. enf. **36**:41 (Jan.) 1933.

5. Leenhardt, E.; Chaptal, J.; Dufoix, M., and Monnier, P.: Néphrose lipoïdique chez un nourrisson de onze mois: Evolution fatal sans hyperuréoémie, Bull. Soc. de pédiat. de Paris **29**:412 (July) 1932.

described also as having comparatively mild cases. The history of one child in this group is reported.

CASE 24.—M. A., a boy, aged 1½ years, was admitted with a history of generalized recurrent edema of two months' duration. There was no hematuria. On admission the child had a temperature of 102 F. and generalized edema. The blood pressure was 80 systolic and 56 diastolic. Examination of the urine showed large amounts of albumin, but microscopic examination revealed only a few formed elements. The chemical analysis of the blood showed a normal blood urea value, a high cholesterol level and a low value for total serum protein. The temperature returned to normal after three days. After one month the edema gradually disappeared. The child remained well, although the albuminuria persisted for five years. At present, eight and one-half years after the onset, the urine is normal.

The second group was comprised of five children whose illness lasted over a longer period. In general, the incidence and severity of

TABLE 1.—*Data on Patients Observed Until Recovery Was Complete*

Case	Age at Onset, Years	Duration of Edema Months	Duration of Albuminuria, Years	Time Observed While Well, Years	Total Observation, Years	Notes
17	3½	12	2	1	3	
23	2¾	10	5	3	8	Peritonitis; improvement after measles
24	1½	3	5	3	8½	
25	8	10	4	3	8	Freedom from albuminuria for 3 years; albuminuria now present
28	3	3	¾	3	4	
30	4	19	3	1½	4½	
34	3	12	1½	2½	4	
38	6	8	1	1	2	Peritonitis and intestinal obstruction
40	3	6	2	8	10	

intercurrent infections were more striking in this group than in the group with a shorter duration of illness. Two of these children had purulent peritonitis, one of whom was operated on. Another had an extensive pneumonic infiltration. These children had clinical symptoms for from one to two years after the onset; the urine contained large amounts of albumin for from one and one-half to five years after the onset.

CASE 23.—J. K., a boy, aged 2¾ years, had a history of generalized edema for ten days. Examination showed generalized edema and large amounts of albumin in the urine, as well as many casts and a few white blood cells. Chemical examination of the blood showed: urea nitrogen, 28 mg. per hundred cubic centimeters; cholesterol, 0.396 per cent, and serum protein, 4.2 per cent. Three days later the urea nitrogen was 16 mg. per hundred cubic centimeters of blood. The blood pressure was always within normal limits. Soon after admission there were clinical signs of involvement of the nasal antrum, although a roentgenogram of the nasal sinuses was normal.

Although the edema varied in amount the child was not free from it at any time during the first six months of his stay in the hospital. Two months after

admission 1,400 cc. of clear fluid was removed by abdominal paracentesis. About three months after admission the child had abdominal pain, and a blood culture was positive for Pneumococcus type IV. The child contracted measles six months after admission. Soon after his recovery from the measles he began to improve and the edema disappeared. While at the hospital he was given a high protein diet. He was also given 0.5 Gm. of thyroid, but without clinical effect.

He has been followed for eight years. The albuminuria persisted for five years. At present he is well.

The reaction of nephrotic patients to infection is varied. Thus, in case 23 measles, occurring during the active phase of nephrosis, apparently inhibited the progress of the nephrosis. Schick [6] mentioned several such cases, and Tezner and Stross [7] reported one case of complete recovery after measles. In patients who have been free from edema for some time, intercurrent infections may be successfully combated without any exacerbation of the nephrosis. One patient (case 17) had appendicitis with peritonitis two years after the onset of illness with no effect on either the urine or the blood. Several other patients had tonsillectomies and various exanthems without deleterious effects.

In the patients who were cured the blood cholesterol value usually returned to normal limits soon after the disappearance of the edema, but occasionally a longer time was required. The albuminuria continued for a longer period.

Great caution must be observed before deciding that a patient has recovered completely. This is illustrated by the following case.

CASE 25.—B. D., a girl, aged 8 years, was admitted with a history of insidious onset of edema five days before admission. The child remained in the hospital almost one year. During this period she had frequently recurring edema and on two occasions had a so-called erysipeloid infection of the skin. She received a high protein diet and at three different periods was given 0.5 Gm. of thyroid a day. On one occasion the administration of thyroid was followed by diuresis. The blood pressure was always normal, and examination of the urine and the blood gave the findings that are usual in cases of lipoid nephrosis. The blood serum protein value was normal when the patient was discharged. Since then the child has led a normal life. Albuminuria persisted for four years, and then for three years the urine was normal. Recently during a routine examination albumin was again found in the urine, although no formed elements were seen microscopically. Chemical examination revealed a urea nitrogen value of 21 mg. per hundred cubic centimeters of blood. The blood pressure was 140 systolic and 95 diastolic. The urinary concentration was normal.

As is revealed by the history, this child has been free from symptoms for seven years and free from albumin in the urine for three years. Recently during a routine examination albuminuria was again found.

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6. Schick, B.: Personal communication.

7. Tezner, O., and Stross, J.: Der Einfluss der Masern und des Nirvanol Exanthems auf der Verlauf der genuinen Nephrose, Monatschr. f. Kinderh. **49**:1 (Jan.) 1932.

There was also a moderate retention of nitrogen and an increase in blood pressure. Is a so-called contracted nephrotic kidney developing, or is some new condition present?

PATIENTS WHO IMPROVED

Seven patients when last seen were free from edema but still had albuminuria. Two of the patients were followed less than a year, three for from one to two years, one for over two years and one for over eleven years. Only one, the child followed for eleven years, is still under observation (table 2). This child's case warrants more complete discussion.

CASE 13.—J. R., a boy, aged 11 years, for about seven years before admission had had chronic osteomyelitis. At the time of admission there was an active focus in one rib. About two weeks before admission, edema was noted for the

TABLE 2.—*Data on Patients Who Inproved, but in Whom Albuminuria Is Still Present*

Case	Age at Onset, Years	Duration of Edema	Total Observation	Notes
3	5	4 mo.	7 mo.	
4	10	10 mo.	1½ yr.	
6	8	17 mo.	20 mo.	
11	3½	6 mo.	15 mo.	
13	11	3½ mo.	11½ yr.	Probably chronic glomerular nephritis; hypertension; no nitrogen retention
14	3	2 yr.	2½ yr.	
27	3	5 mo.	7 mo.	

first time. Examination revealed a well nourished child with generalized edema, which recurred during the following three months. The urine contained large amounts of albumin and many casts. Examination of the blood showed urea nitrogen, 14 mg. per hundred cubic centimeters; cholesterol, 0.62 per cent, and serum protein, 3.5 per cent. The blood pressure was 130 systolic and 70 diastolic. Concentration tests showed a maximum specific gravity of the urine of 1.014.

The osteomyelitis of the rib was entirely healed in eight months, and since then no new lesion has developed. Three years after discharge the boy was readmitted to the hospital with a complaint of substernal pain following acute pharyngitis. Examination showed a short systolic murmur at the apex, and an electrocardiogram revealed a prolonged P R interval. The P R interval was normal within a week. At this time the chemical examination of the blood gave entirely normal results, and the patient was discharged with a diagnosis of rheumatic fever. Since then this patient, now aged 23, has developed normally; he now weighs 164 pounds (74.5 Kg.). The systolic murmur at the apex has disappeared. The blood pressure, however, is still increased, being about 140 systolic and 106 diastolic. The urine contains large amounts of albumin, and a recent microscopic examination showed a few formed elements. The urinary concentration is more nearly normal. The maximum specific gravity is 1.022. The chemical examination of the blood gave normal results. An electrocardiogram showed left ventricular preponderance.

A decision as to the diagnosis in this case is difficult to make. At the time of the first admission amyloid nephrosis was considered because of the protracted osteomyelitis. After years of observation we believe that this is a case of progressive glomerular nephritis.

PATIENTS WHO DID NOT IMPROVE

There were two patients who still had manifest edema and albuminuria when last seen. One patient was observed for over two years and the other for over six months. The ultimate outcome was of course unknown.

PATIENTS WHO DIED

Eighteen children were followed until they died. It is well known that death in the course of lipoid nephrosis is usually due to an intercurrent infection involving the peritoneum or respiratory tract. Necropsies showed that seven of the children had peritonitis and that one child had pneumonia together with meningitis. Of the other nine children, eight had peritonitis and one died of diphtheria after the nephrotic condition was much improved. The organisms obtained from the infected peritoneum were a pneumococcus in ten cases and a streptococcus in three cases (table 3).

We can discuss with some assurance the nine cases in which necropsies were made. Six of these children were ill for less than seven months. Three others were ill for two years, three years and three and three-fourth years, respectively. The cases can also be divided into those of short duration and those of long duration. We have attempted to correlate the postmortem observations regarding the kidney with the duration of the disease. In all cases, both of short and of long duration, there were varying degrees of degeneration in the tubules. However, those of short duration, as was reported many years ago by Fahr [8] and later by Wolbach and Blackfan [9] and others, presented little or no change. Those of longer duration usually showed changes in the glomeruli and in the interstitial tissue. The following case is typical of the cases of short duration.

CASE 35.—M. D., a boy, aged 5 years, was admitted with a history of gradually increasing generalized edema of six weeks' duration. The urine contained a large amount of albumin, but microscopic examination showed very few formed elements. Examination of the blood showed: urea nitrogen, 10 mg. per hundred cubic centimeters; cholesterol, 0.665 per cent, and serum protein, 4.9 per cent. The blood pressure was 104 systolic and 50 diastolic. A roentgenogram of the nasal sinuses showed clouding of both ethmoid sinuses and both antrums.

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8. Fahr, T.: Ueber Nephrose, Deutsches Arch. f. klin. Med. **125**:66 (March 5) 1918.

9. Wolbach, S. B., and Blackfan, K. D.: Clinical and Pathological Studies on So-Called Tubular Nephritis (Nephrosis), Am. J. M. Sc. **180**:453 (Oct.) 1930.

The child was given a high protein diet and also 0.5 Gm. of thyroid at intervals. Recurrent edema persisted. Three and one-half months after admission abdominal pain and symptoms of peritonitis developed, and the patient died within five days.

Necropsy revealed purulent peritonitis. The heart muscle was normal, but several golden yellow patches, about 2 mm. in diameter, were seen beneath the endothelium of the anterior leaflet of the mitral valve. The mouth of the coronary

TABLE 3.—*Data on Patients Who Died*

Case	Age at Onset, Years	Total Duration	Fatal Intercurrent Infection: Site	Fatal Intercurrent Infection: Bacteriology	Notes and Postmortem Observations
15	2	4½ mo.	Peritoneum	Streptococcus haemolyticus	Kidneys large; glomeruli normal; tubular swelling; some interstitial infiltration
19	2	6 mo.	Peritoneum	Pneumococcus I	Kidneys large; glomeruli normal; tubular swelling; atherosclerotic changes in aorta
20	4	3 yr.	Peritoneum	Pneumococcus IV	Kidneys large; occasional fibrous glomerulus; tubular swelling
22	9	3¾ yr.	Peritoneum	Pneumococcus IV	Kidneys large; rare thickening of Bowman's capsule and adherent cusps; rare calcified tubule
29	2½	4 mo.	Peritoneum	Pneumococcus IV	Kidneys large; glomeruli normal; tubular swelling
31	2	4½ mo.	Peritoneum	Streptococcus viridans	Kidneys large; glomeruli normal; tubular swelling; blood cholesterol never increased
35	5	5½ mo.	Peritoneum	Pneumococcus	Kidneys large; glomeruli normal; tubular swelling; few atherosclerotic changes in aorta
36	2½	4 mo.	Peritoneum and meninges	Pneumococcus	Kidneys large; glomeruli normal; tubular swelling
37	11	2 yr.	.....	.....	Kidneys large; hyalinized glomeruli; tubular swelling; diffuse atherosclerotic changes; thrombosis of right middle cerebral artery
1	4	5 mo.	Lung		
2	11	7 mo.	Peritoneum	Pneumococcus	
9	5	11 mo.	Pharynx	Diphtheria	Much improved when infected with diphtheria
10	7	18 mo.	Peritoneum	.....	Died at home
12	7	2 mo.	Peritoneum	Pneumococcus I	
18	3	20 mo.	Peritoneum	Pneumococcus II	
26	2	9 mo.	Peritoneum	Pneumococcus IV	
39	2	3 mo.	Peritoneum		
41	3	6 mo.	Peritoneum	Streptococcus haemolyticus	

arteries and the intimal surface of the ascending aorta showed a few scattered yellow elevated patches. The kidneys were large, the cortex was widened and numerous yellow streaks were seen traversing the medulla and the cortex.

Microscopic examination of the kidneys showed the glomeruli to be normal. An azan-carmine stain showed slight thickening of the basement membrane but no tuft adhesions or proliferation of the endothelial cells of the glomeruli. The convoluted tubules were swollen and many of them were filled with leukocytes.

In children who died after a longer period there were changes in the interstitial tissue and often some degenerative (noninflammatory)

changes in the glomeruli. At necropsy the kidneys did not resemble those of a person with chronic inflammatory nephritis. There was also focal scarring or infiltration in the interstitial tissues and some hyalinization of the glomerulus where a tubule had been obliterated.

The following case of longer duration, in addition to the typical pathologic findings, shows certain points of clinical interest. The finding of a few red blood cells, a transient increase of blood pressure or moderate retention of blood nitrogen did not necessarily invalidate the diagnosis of nephrosis. When the patient was admitted to the hospital, a moderate increase in blood pressure or in retention of blood nitrogen was occasionally found. After a short period the blood pressure and the retention of blood nitrogen returned to normal limits.

CASE 22.—S. M., a boy, aged 9 years, gave a history of insidious development of edema for six weeks before admission. His past history was unimportant. There was generalized edema, as well as a large amount of albumin and a large number of casts in the urine. The chemical examination of the blood showed: urea nitrogen, 19.6 mg. per hundred cubic centimeters; cholesterol, 0.628 per cent, and serum protein, 4.2 per cent. The blood pressure was 100 systolic and 80 diastolic.

After two months the boy was discharged from the hospital with no manifest edema. At the end of six months the edema reappeared and lasted for several weeks. It reappeared again after three months. He was then free from edema for eighteen months, at which time he had symptoms of peritonitis. A blood culture at this time was positive for Pneumococcus type III. He also had an erysipeloid lesion in the lumbar region which eventually became fluctuant and from which a pneumococcus was recovered. During the next six months there was recurrent edema, and the patient finally succumbed to a pneumococcic peritonitis.

On rare occasions while this patient was under observation, a slight increase in blood pressure was noted. At times there was a moderate retention of blood urea nitrogen, the content becoming normal within a few days. The blood cholesterol was usually increased, the lowest value being 0.218 per cent. In the latter part of the illness the serum protein content was normal, despite the fact that there were always large amounts of albumin in the urine.

Necropsy showed fluid in both pleural cavities. The peritoneal cavity contained about a liter of purulent fluid. The size of the kidneys was twice that usually found in a body of this size. The cortex was wider than usual.

Microscopic examination of the kidneys showed diffuse tubular degeneration and moderate dilatation of the lumens of the tubules. In numerous places the tubular cells had undergone calcification. In one or two areas, Bowman's capsule was definitely thickened and the glomerular tufts were adherent. There were likewise numerous linear areas of round cell infiltration in the cortex. A sudan III stain infiltrated many of the descending Henle loops; some primary convoluted tubules showed amorphous masses of calcium plugging the lumens. There was a rich and abundant deposit of neutral fat in many of the convoluted tubules. Masses of fat were contained in the lumens and others in wandering cells. Fatty deposition was not diffusely distributed, but was rather patchy. The epithelium of the tubules was completely necrotic and was infiltrated by droplets of neutral fat in some areas. In areas such as these, interstitial infiltration was especially marked.

This child was free from edema at one period for over fifteen months. This illustrates how guarded one must be in prognosis. This boy had had peritonitis several times and an erysipeloid lesion from which a pneumococcus was recovered.

Atherosclerotic changes, though occasionally occurring in cases of short duration, are found more frequently in those of longer duration. One of our patients showed such extensive atherosclerotic changes that we will describe his case in more detail. This case is also important because the child died suddenly while free of evident edema and without any intercurrent infection. To the best of our knowledge, this is the first necropsy to be reported in which the patient at the time of death was free from edema and did not have an intercurrent infection. Therefore, the lesions that were found in the kidney, especially those in the convoluted tubules, cannot be attributed to an intercurrent infection.

CASE 37.—S. K., a boy, aged 11 years, was admitted with a history of intermittent edema for five months. Physical examination showed generalized edema. The urine contained large amounts of albumin with many casts and a few red blood cells. Chemical examination of the blood showed: urea nitrogen, 29 mg. per hundred cubic centimeters; cholesterol, 0.45 per cent, and total serum protein, 5.2 per cent. The blood pressure was 110 systolic and 75 diastolic.

Shortly after hospitalization the child was operated on for peritonitis, and pneumococcus of type IV was obtained. He was discharged after two months. For the next two years he was seen at frequent intervals and the edema gradually disappeared. He was on a high protein diet and took 0.3 Gm. of thyroid daily. The blood pressure remained normal. Albuminuria persisted, and two months before his death the blood urea nitrogen was 19 mg. per hundred cubic centimeters, the cholesterol, 0.4 per cent, and the total serum protein, 6.12 per cent.

Except for coryza, this child was in good health until the day of his readmission, when he complained of severe headache and then collapsed. He was admitted to the hospital in a semistuporous condition. Physical examination revealed paralysis of the left side of the face, left arm and left leg. There were also cyanosis and swelling of the left upper extremity. An examination of the fundi of the eyes showed complete blocking of the right central artery of the retina. Chemical examination of the blood showed a urea nitrogen value of 15 mg. per hundred cubic centimeters. The blood pressure was 160 systolic and 130 diastolic. He died soon after admission.

Macroscopic Postmortem Examination.—Lungs: The lungs were normal; the pulmonary vessels contained a few linear streaks and slightly elevated yellow plaques.

Heart and Vessels: The pericardium was smooth and glistening and contained no fluid. The heart was slightly enlarged to left and right and was flabby. The auricles and valves were grossly normal. The left ventricular endocardium was thickened and yellowish. Both ventricles were moderately dilated, and the left showed slight thickening of the wall, with hypertrophy of the papillary muscles and rounding of the trabeculae carneae. The myocardium was apple red and showed no tigering. The coronary arteries, especially in the wider portions, showed many intimal deposits of yellowish material, often as streaks, often as definitely raised plaques, and in the left anterior descending coronary artery there

was definite, extreme narrowing of the lumen, extending for a distance of about 3 mm. The aorta throughout its extent presented many linear streaks and raised plaques of yellowish intimal deposits, especially at its root. These deposits extended into some of the branches, notably the iliac and femoral arteries. On the right wall of the innominate artery, just above its ostium, was a grayish, ragged, friable nodule, the size of a split pea, firmly adherent to the wall of the vessel. On the left wall, somewhat superiorly, was a similar parietal thrombus, about 6 mm. in diameter. The branches of the innominate, the right common carotid and the right subclavian artery showed no changes. The right axillary artery was normal, but just where it becomes the right brachial, the lumen was found to be plugged for about 1½ inches (4 cm.) by a firm, grayish, friable plug with a conical tail pointing proximally. In the region of the antecubital fossa another embolus was seen in the brachial artery. A large branch of the axillary artery was also occluded just beyond its origin by a gray adherent embolus. The left common carotid and left subclavian arteries showed no changes.

Kidneys: The kidneys were slightly enlarged, soft and flabby. The capsule stripped easily, revealing a smooth reddish-yellow surface. On section the surface was very yellow and opaque, with indistinct though recognizable markings. The cortex was of normal width. The renal vessels showed no changes except in the inferior branch of the left renal vein, where there was a flat, ragged, grayish, friable parietal thrombus about 3 mm. in diameter, firmly adherent to the wall but not obstructing the lumen.

Microscopic Postmortem Examination.—Aorta: The intima appeared to be normal. It was composed of more or less homogeneous ground substance and contained cells with large vesicular nuclei, except at several points where there were thickening and vacuolation of the intima with a deposition of fat and an invasion of fibroblasts and round cells. The media showed narrowing and was traversed by blood vessels. At several points the elastic tissue was interrupted and in great part destroyed, and reduplications also occurred. In the slide of the abdominal aorta were noted several areas of destruction of the elastic tissue where the intimal thickening was not excessive. Staining showed a marked hyperplasia of the intima and areas of deposition of fat, which were maximal in the internal elastic tissue; and on the external side there was severe destruction of the medial elastic tissue with deposition of fat in the affected areas. Medial damage was most marked where intimal hyperplasia and deposition of fat were greater.

Heart: The heart muscle showed a very fine deposition of fat in many areas. The right coronary artery showed hyperplasia with thickening, which amounted to twice the thickness of the media and was composed of fibrocytes. New elastic tissue formation in the intima was extensive, with diffuse fatty deposition in the intima and in certain parts of the media.

Brachial Artery: The lumen was filled by an onion peel embolus. Polymorphonuclear leukocytes and red blood cells were numerous. The arterial wall was normal.

Kidneys: The capsule was regular. There were frequent small areas of collapsed and atrophic tubules with pyknotic nuclei and a few round cells and polymorphonuclear cells. Near these the glomeruli were fibrosed or hyalinized. Throughout were scattered glomeruli in various stages of hyalinization or fibrosis. Frequently there was a thick crescent of fibrous tissue, but the capsular basement membrane was well preserved. A few glomeruli were replaced by large basophilic cells with large vesicular nuclei. Some tubules were atrophic, and a few were calcified, but most of them were swollen. The endothelial cells were large. The large arteries showed slight hyperplasia of the intima and little change in the

elastic tissue, although some of the medium-sized arteries showed reduplication. Stains showed fat in the media and in the intima of the arteries and arterioles and also in the endothelium as well as in the glomeruli and in the crescents of fibrosed glomeruli.

Brain: The brain showed a complete thrombosis of the right middle cerebral artery.

SPECIAL FEATURES

Infections of the accessory nasal sinuses did not seem to be an important factor in our cases. Each patient was carefully examined in the rhinolaryngologic department. Roentgenograms were also made. In only six cases did we feel that there was any involvement of the sinuses. Only two of these patients had clinical evidence of acute disease of the sinus.

In the complicated clinical picture presented by nephrosis, efforts have been made to correlate certain clinical and laboratory data. We will discuss this in a later communication. Nevertheless, by way of completeness, we record our results.

1. There was no constant relationship between the height of the blood cholesterol level and the basal metabolic rate.

2. There was also no constant relationship between the total serum proteins and the patient's weight.

3. There was no constant relationship between the body weight (edema) and the blood cholesterol content.

4. When the serum protein value was low the cholesterol content was usually high, but even this was not constant. It is therefore evident that an increased blood cholesterol content does not always take the place of the proteins lost from the blood.

5. In cases with a low serum protein value, it is usually the albumin that is excreted. However, in several cases in which the serum protein value was low, the expected reversal of the albumin-globulin ratio was not always found.

6. There was no constant relationship between the intensity of the edema and the amount of protein lost in the urine.

7. The blood cholesterol content often remained high after all signs of edema had disappeared. However, in many cases the cholesterol content became normal soon after the disappearance of the edema and stayed normal.

TREATMENT

In regard to treatment we have little to add to what has been said so often by others. As was first advocated by Epstein,[10] every patient

10. Epstein, A. A.: The Nature and Treatment of Chronic Parenchymatous Nephritis (Nephrosis), J. A. M. A. **69**:444 (Aug. 11) 1917.

was given a diet high in protein and low in sodium chloride. This diet was kept up indefinitely. There was no restriction as to fluids.

We do not agree with Epstein [11] that thyroid therapy has any constant effect. Some of our patients seemed, at times, to respond to thyroid medication and at other times there was no response. One patient received 0.5 Gm. of thyroid daily without effect for over three years. Other patients were given as much as 1.5 Gm. a day without apparent effect. It is possible that in some of our cases the thyroid dosage was not large enough or that it was not given for a long enough period of time.

We cannot express any opinion as to the treatment which was recently advocated by Schiff.[12] He commenced his treatment with raw fruit and certain raw vegetables, which were continued until diuresis began, when as many as five egg yolks with sugar and orange were given. This treatment was tried by us in two cases without any apparent effect.

COMMENTS

In this communication we have attempted to emphasize the course and prognosis of a clinical entity known as lipoid nephrosis in a group of patients carefully followed over many years. Half of the children died. About 25 per cent of the children seem to have recovered. If these children continue to remain well over an additional period of years, this will be further evidence that lipoid nephrosis is a clinical entity from which recovery is possible. The remaining 25 per cent either gave no clinical symptoms of nephrosis but showed albuminuria or were obviously unimproved. In the literature a number of individual cases are reported, but the most comprehensive series to our knowledge is that of Davison and Salinger.[13] In a series of twenty cases there were six deaths, six patients recovered and eight were improved. Wolbach and Blackfan [9] reported ten deaths among twenty-one patients. Clausen [14] reported thirteen deaths among twenty-eight patients. Abraham [15] reported eighteen deaths among thirty-four patients; of the remaining sixteen, three recovered and seven were improved.

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11. Epstein, A. A.: Further Observation on the Nature and Treatment of Chronic Nephrosis, Am. J. M. Sc. **163**:167 (Feb.) 1922; Thyroid Therapy and Thyroid Tolerance in Chronic Nephrosis, J. A. M. A. **87**:913 (Sept. 18) 1926.

12. Schiff, E.: Ueber die Lipoidnephrose im Kindesalter: Ernährungstherapie und einige klinische Beobachtungen, Jahrb. f. Kinderh. **137**:1 (Oct.) 1932.

13. Davison, W. C., and Salinger, R.: Tubular Nephritis (Nephrosis) in Children and Its Relationship to Other Forms of Nephritis, Bull. Johns Hopkins Hosp. **41**:329 (Dec.) 1927.

14. Clausen, S. W.: Nephritis in Children, Atlantic M. J. **29**:201 (Jan.) 1926.

15. Abraham, I.: Ueber den Ausgang der im Kindesalter beginnenden genuinen Nephrose, Monatschr. f. Kinderh. **53**:329 (June 9) 1932.

In analyzing these cases one receives the impression that recovery from lipoid nephrosis depends on the ability either to escape or to recover from a severe secondary infection. The nephrotic symptoms are not cumulative. We must agree, therefore, with Epstein [10] and others that nephrosis is not an inflammatory disease of the kidney. Many children seem to recover completely, and in fatal cases little or no inflammatory changes are seen after several years of illness. The kidneys in lipoid nephrosis are so unlike those in subacute or chronic glomerular nephritis that we feel that it is not the same disease. However, we must make this statement with certain reservations, since one of our patients who was free from albuminuria for three years subsequently had a return of the albuminuria, with a moderately increased blood nitrogen value and a moderately increased blood pressure. This child is still clinically well.

While it may be true that a clinical diagnosis of lipoid nephrosis is difficult at times, we feel that if a patient can be followed for a number of months a correct diagnosis can be made with a fair degree of accuracy. At the onset, subacute glomerular nephritis may resemble lipoid nephrosis, but its subsequent course is entirely different. Subacute glomerular nephritis usually progresses to a fatal termination. The blood in such cases shows a progressively increased retention of nitrogen with or without high pressure, and there are large amounts of albumin and many formed elements in the urine. As in lipoid nephrosis, the total serum protein level is usually low and the blood cholesterol content is high. At necropsy, a kidney from a patient with subacute nephritis may resemble that from a patient with lipoid nephrosis macroscopically, but microscopically the difference is very evident.

A comprehensive summary of the controversy as to whether the lesion in the kidney in a typical case of lipoid nephrosis is degenerative or inflammatory was given by McElroy.[16] Bell [17] and McGregor [18] stated that with the usual stains the glomeruli may appear to be normal, but when special stains are used some inflammatory changes can be seen in the endothelial nuclei or basement membrane. Kantrowitz and Klemperer [19] reported two cases in which these special stains revealed no inflammatory changes. Case 29 in our study is such a case. Wolbach and Blackfan [9] also stated that the glomerular changes are not inflam-

16. McElroy, J. B.: Nephroses, J. A. M. A. **89**:940 (Sept. 17) 1927.

17. Bell, E. T.: Lipoid Nephrosis, Am. J. Path. **5**:587 (Nov.) 1929.

18. McGregor, L.: The Cytological Changes Occurring in the Glomerulus in Clinical Glomerulonephritis, Am. J. Path. **5**:559 (Nov.) 1929.

19. Kantrowitz, A. R., and Klemperer, P.: Ueber Lipoidnephrose, Virchows Arch. f. path. Anat. **280**:554 (March) 1932.

matory. Mackay and Johnston [20] and Ehrich [21] reported the clinical findings and the postmortem observation in a boy with a history of seventeen years of illness. This patient died of peritonitis. At necropsy a large kidney was found with some degenerative changes in the convoluted tubules and glomeruli.

The question of atherosclerotic changes in this disease are of great interest. One patient (case 37) with a typical history of lipoid nephrosis of two years' duration had most extensive arteriosclerotic changes. Anitschkov [22] stated that atherosclerosis is not essentially degenerative, but rather infiltrative. He also states that in experimental atherosclerosis, lipoid substances (which are abundant in the blood of cholesterolized animals) together with the nutritive lymph stream invade the arterial wall directly from the lumen of the vessel. Early human and early rabbit lesions are similar grossly and microscopically. In experimental arteriosclerosis there is no fatty infiltration of the elastic fibers or lamellae, as is seen in human subjects. What happens to the atherosclerotic changes in the patients who recover? It is probable that when the blood cholesterol content becomes normal the atherosclerotic deposits are absorbed. In other words, this may be a reversible reaction.

SUMMARY

Thirty-six children who were considered at some time to have true lipoid nephrosis were seen over a period of fifteen years. These patients were carefully observed and followed.

Nine children (25 per cent) seem to have recovered completely. These were followed for from two to ten years. The albuminuria persisted for from one to five years after the disappearance of the edema. However, the reservation must be made that an even longer observation may be necessary, since in one of our patients there was a return of albuminuria after three years. This albuminuria, now present, may not necessarily be due to nephrosis.

Seven children when last seen were considered to be improved. There was no evidence of edema, but albuminuria was still present. These children were followed for from seven months to eleven and one-half years.

Two children were unimproved when last seen.

Eighteen patients (50 per cent) were followed until death. On nine of these necropsy was performed.

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20. Mackay, E. M., and Johnston, C.: Lipoid Nephrosis; Report of a Case of Unusual Duration, Arch. Int. Med. **45**:734 (May) 1930.

21. Ehrich, W.: Lipoid Nephrosis of Unusual Duration, Arch. Int. Med. **45**: 749 (May) 1930.

22. Anitschkov, N.: Arteriosclerosis: A Survey of the Problem, New York, The Macmillan Company, 1933, p. 271.

The children could be grouped clinically into those having symptoms of comparatively short duration and those with symptoms of long duration.

Three patients have been discussed in detail: (*a*) A child who was symptom-free for seven years and without albuminuria for three years, but who at present has a return of albuminuria. There is also a moderate increase in blood pressure as well as a slight increase in blood urea nitrogen value. (*b*) A patient observed for eleven and one-half years in whom albuminuria has persisted. This boy also has hypertension but no retention of blood nitrogen. His case is probably one of chronic glomerular nephritis. (*c*) A child who died suddenly of thrombosis of the cerebral artery. This child was the first patient with lipoid nephrosis on whom autopsy was performed at the time of death who was free from edema and did not have an intercurrent infection.

In analyzing our cases one receives the impression that recovery from lipoid nephrosis depends on the ability of the patient either to escape or to recover from a severe secondary infection.

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METABOLISM IN CHILDREN DURING MUSCULAR WORK

I. THE EFFECT OF RACING ON THE URINARY CONSTITUENTS IN BOYS

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Nothing is more enjoyable than the promoting of physical education. However, it must be borne in mind that exercise without due regard to hygiene not only fails to do good but actually injures the health and weakens the chances of making athletic records. Many deplorable results, we regret to say, are still observable today because persons have become so absorbed in the encouragement of exercise that they disregard all scientific medical advice. Physical education should never be divorced from the science of nutrition. A child must be properly nourished in order to obtain good results from exercise.

Recently, remarkable progress has been made by means of a careful study of the physical influence of exercise, for instance, changes of metabolism due to exercise. The metabolic changes caused by muscular work come within the range of the science of nutrition as well as of the hygiene of athletics. Studies of the changes in metabolism have been carried out for adults, but if the metabolic changes observed in adults are not the same as those that occur in children, it is dangerous to apply to children the conclusions reached in studies on adults. We therefore undertook a study of metabolism during muscular work in children. The first aspect investigated the effect of running races on the urinary constituents of boys.

EXPERIMENTS

Three different experiments were made:

1. On Oct. 12, 1933, the changes in the urinary constituents after exercise were observed in thirty-seven boys from 7 to 13 years of age who took part in a short distance (40, 60 or 135 meter) or a long distance (1,200 meter) race at an athletic contest held at the Kagomati primary school (table 1).

2. Nov. 5, 1933, seven boys from 11 to 12 years of age and three men from 21 to 24 years of age ran a race similar to that in the first experiment and urinated five times at thirty minute intervals before and after the race (table 2).

3. On Dec. 10, 1933, two 12 year old boys ran a similar race and urinated nine times at thirty minute intervals (table 3).

In these three experiments, none of the boys or men perspired noticeably.

From the Imperial Government Institute for Nutrition, Koisikawa-Ku, Tokyo.

TABLE 1.—*Changes in the Urinary Constituents in Boys After Short Distance and Long Distance Races* *

Name	Age, Years	Weight, Kg.	Pulse Rate		Total Nitrogen, Gm.‡		Phosphorus, Mg. per Cc.	
			Before	After	Before	After	Before	After
First Grade (40 Meter Race)								
S. W.	7	17.0	100	90	2.4	2.9	...	...
Y. K.	7	19.0	80	98	8.6	6.0	...	...
H. T.	8	16.0	108	106	9.0	7.4	...	...
Average.....		17.3	96	98	6.7	5.4		
Second Grade (60 Meter Race)								
T. H.	9	21.5	94	100	11.6	7.4	...	...
I. J.	9	20.7	100	94	8.7	8.1	...	...
I. T.	8	20.7	106	124	6.0	1.3	...	...
M. N.	9	23.2	86	104	9.7	8.9	...	...
E. M.	9	21.2	106	130	9.7	9.6	...	...
Average.....		21.5	98	110	9.1	7.1		
Third Grade (60 Meter Race)								
S. T.	10	24.6	80	124	9.6	9.5	...	...
A. D.	10	23.4	90	86	8.0	8.9	...	...
Y. K.	9	27.0	100	126	5.0	5.9	...	...
O. D.	10	23.5	82	110	13.9	12.5	...	...
S. K.	10	23.0	120	128	9.0	9.5	...	...
Average.....		24.3	94	115	9.1	9.3		
Fifth Grade (135 Meter Race)								
S. T.	12	33.4	94	...	2.4	0.8	0.4	3.4
Y. G.	11	25.4	108	...	6.2	±6.4	1.2	1.6
K. I.	12	29.8	92	...	7.3	8.4	1.8	1.6
S. M.	12	25.2	102	112	8.0	8.7	1.3	1.8
Y. D.	12	25.5	...	...	3.7	7.6	0.9	1.6
M. M.	12	30.6	...	118	9.1	16.5	1.7	2.3
O. W.	12	26.5	110	...	8.0	+13.0	1.6	3.7
Average.....		28.1	101	115	6.4	8.8	1.3	2.3
Sixth Grade (135 Meter Race)								
N. Y.	13	27.4	78	104	7.7	7.3	...	...
I. K.	13	31.0	..	100	7.9	2.3	...	...
I. H.	13	26.0	81	104	2.9	3.2	...	...
S. D.	13	48.9	82	102	4.8	3.4	...	...
M. S.	13	28.3	60	...	4.0	4.8	...	...
H. D.	13	33.0	88	100	3.2	2.3	...	...
F. N.	13	30.5	..	84	3.9	2.3	...	...
O. H.	13	28.8	70	108	5.6	4.3	...	...
I. S.	12	27.7	82	120	7.8	5.1	...	...
K. B.	13	28.4	90	100	4.2	1.5	...	...
O. Y.	13	35.1	76	136	9.6	5.1	...	...
O. S.	13	36.0	86	130	7.3	6.9	...	...
H. E.	13	32.5	85	106	8.4	5.5	...	...
I. K.	13	36.0	84	84	2.9	1.3	...	...
Average.....		32.1	80	106	5.7	4.0		
Fifth Grade (1,200 Meter Race)								
Y. S.	12	30.2	78	...	3.2	+2.5	0.3	1.5
M. M.	12	30.6	..	...	4.2	+5.1	0.3	1.0
Y. G.	11	25.4	86	126	5.3	+5.6	0.6	2.1
T. H.	12	27.0	98	120	5.4	+6.5	0.9	3.6
O. W.	12	26.5	82	116	4.7	+6.7	0.4	2.7
Y. D.	12	25.5	88	126	4.4	+3.2	0.5	1.1
K. I.	12	29.8	94	104	6.1	+4.7	0.8	1.7
K. J.	12	30.2	86	134	2.9	+2.9	0.3	1.0
S. T.	12	33.4	86	124	2.9	+2.3	0.5	0.9
Average.....		28.7	87	121	4.3	4.4	0.5	1.7
Sixth Grade (1,200 Meter Race)								
			1 2		1 2			
H. E.†	13	32.5	85 106	140	8.4 5.5	+5.7		
I. H.	13	26.0	81 104	134	2.9 3.2	+6.6		
S. D.	13	48.9	82 102	116	4.8 3.4	+3.5		
O. S.	13	36.0	86 130	130	7.3 6.9	+6.3		
I. S.	12	27.7	82 120	128	7.8 5.1	+8.4		
I. K.	13	31.0	.. 100	108	7.9 2.3	+4.7		
M. S.	13	28.3	60 ...	104	4.0 4.8	+3.0		
O. H.	13	28.8	70 108	110	5.6 4.3	+5.1		
K. B.	13	28.4	90 100	146	4.2 1.5	+3.8		
I. K.	13	36.0	84 84	114	2.9 1.3	+5.2		
O. Y.	13	35.1	76 136	126	9.6 5.1	+4.9		
H. D.	13	33.0	88 100	126	3.2 2.3	+2.9		
F. N.	13	30.5	.. 84	110	3.9 2.3	+4.8		
Average.....		32.5	80 106	122	5.6 3.7	5.0		

* In tables 1 to 3 are recorded the data obtained at thirty minute intervals before and after the races.

† The winner's time was six minutes, thirty seconds.

‡ In tables 1 to 3 + represents obvious albuminuria; ±, obscure albuminuria.

TABLE 2.—*Changes in the Urinary Constituents in Boys and Men After a 1,200 Meter Race*

	Boys							
Name	Y. S.*	M. M.	Y. G.	T. H.	O. W.	Y. D.	K. I.	Average
Age	12	12	11	12	12	12	12	
Weight, Kg.	30.9	30.5	26.2	27.8	27.9	25.9	30.3	28.5
Pulse rate								
Before: 1	76	102	92	96	90	92	84	90
2	84	98	86	98	88	88	86	90
After: 1	126	130	138	120	102	128	130	126
2	100	120	108	106	100	120	106	109
3	88	110	110	116	98	108	80	101
Respiratory rate								
Before	22	18	24	26	24	22	22	23
After: 1	42	32	34	34	34	30	26	33
2	26	16	22	24	22	18	20	21
3	20	14	22	20	24	22	20	20
Total urine, cc.								
Before: 1	47	14	30	13	28	8	17	22
2	60	16	23	14	32	8	15	24
After: 1	+38	+20	+22	20	27	+15	+18	23
2	±12	±8	13	12	11	+7	±8	10
3	10	10	16	12	12	7	9	11
Total nitrogen, mg.								
Before: 1	152.8	128.4	118.3	133.5	173.2	101.4	124.2	133.1
2	158.2	174.9	127.4	162.2	197.7	106.5	135.2	151.7
After: 1	69.4	103.1	99.7	133.5	113.2	92.2	88.7	100.0
2	63.4	66.7	98.8	114.1	131.0	67.2	73.5	87.8
3	76.4	114.1	116.6	151.2	154.6	104.8	106.5	117.7
Phosphoric acid, mg.								
Before: 1	18.2	18.2	24.1	22.1	17.6	15.6	15.6	18.8
2	18.0	25.4	27.1	26.0	17.6	17.6	15.0	21.0
After: 1	37.2	35.8	46.2	47.5	26.0	35.8	32.5	37.3
2	24.7	30.6	23.4	20.2	16.3	25.9	23.4	23.5
3	12.2	20.8	26.0	21.5	15.6	15.6	16.3	18.3
Creatine, mg.								
Before: 1	0.1	1.3	1.0	1.5	1.3	0.0	0.0	0.7
2	0.0	1.1	0.5	1.8	0.8	0.0	0.0	0.6
After: 1	0.1	1.0	0.5	1.4	0.3	0.2	0.0	0.5
2	0.6	0.5	0.5	1.1	0.1	0.4	0.6	0.5
3	0.3	0.4	0.3	0.8	0.1	0.5	0.5	0.4
Creatinine, mg.								
Before: 1	6.1	6.0	4.9	5.6	5.4	6.0	5.8	5.7
2	6.5	6.0	4.6	4.9	5.4	4.9	5.4	5.4
After: 1	4.3	4.1	4.1	4.6	4.6	4.2	4.2	4.3
2	5.3	5.5	4.5	4.9	5.2	5.1	5.4	5.1
3	4.8	5.9	4.5	5.2	5.1	5.1	5.3	5.1

	Men			
Name	S. M.	A. K.	T. N.	Average
Age	21	22	24	
Weight, Kg.	48.7	51.3	50.9	50.3
Pulse rate				
Before: 1	88	70	84	81
2	86	..	..	86
After: 1	116	116	106	113
2	110	88	106	101
3	102	80	96	93
Respiratory rate				
Before: 1	16	18	20	18
After: 1	22	24	26	24
2	18	16	20	18
3	16	16	16	16
Total urine, cc.				
Before: 1	21	21	16	19
2	19	17	20	19
After: 1	+46	±60	+36	47
2	+24	24	21	23
3	+11	17	9	12
Total nitrogen, mg.				
Before: 1	199.4	202.8	173.2	191.8
2	209.5	167.3	198.5	191.8
After: 1	152.1	212.9	114.9	160.0
2	139.4	146.2	127.6	137.7
3	149.5	157.1	109.0	138.5
Phosphoric acid, mg.				
Before: 1	36.4	20.8	17.6	24.9
2	30.6	14.3	15.6	20.2
After: 1	58.5	55.4	37.1	50.3
2	57.2	33.2	31.9	40.8
3	15.6	14.3	9.8	13.2
Creatine, mg.				
Before: 1	0	0	0	0
2	0.0	0.2	0.0	0.1
After: 1	0.2	0.5	0.0	0.2
2	0.3	0.1	0.1	0.2
3	0.3	0.1	0.1	0.2
Creatinine, mg.				
Before: 1	10.9	10.1	9.5	10.2
2	9.5	9.3	9.5	9.4
After: 1	6.8	10.8	7.7	8.4
2	8.5	10.8	10.1	9.8
3	8.6	11.5	10.1	10.1

* The winner's time was six minutes and thirty-seven seconds.

It goes without saying that food has a great influence on the urinary constituents, but the reports published heretofore have paid no attention to this point. In our second and third experiments due consideration was given to this factor; in the second experiment we supplied the same diet qualitatively, and in the third experiment the boys were kept at the institute for two days before the race and were supplied with the same diet qualitatively as well as quantitatively.

The urine was analyzed quantitatively and qualitatively.

TABLE 3.—*Changes in the Urinary Constituents in Two Boys After a 1,200 Meter Race*

Name		M. M.	Y. S.*	Aver.
Age		12	12	
Weight, Kg.		30.35	30.80	30.58
Pulse rate				
Before:	1	88	72	80
	2	87	70	79
	3	84	72	78
After:	1	148	133	141
	2	96	92	94
	3	98	76	87
	4	90	80	85
	5	84	72	78
Respiratory rate				
Before:	1	18	22	20
	2	18	23	21
	3	18	23	21
After:	1	26	30	28
	2	20	24	22
	3	18	18	18
	4	17	20	19
	5	19	23	21
Total urine, cc.				
Before:	1	33	27	30
	2	31	22	27
	3	31	18	25
After:	1	+25	+31	28
	2	14	+13	14
	3	6	±14	10
	4	37	14	26
	5	22	±14	18
	6	17	14	16
Total nitrogen, mg.				
Before:	1	240.0	241.6	240.8
	2	218.8	219.7	219.3
	3	227.3	203.6	215.5
After:	1	123.3	126.6	125.0
	2	125.0	119.8	127.4
	3	40.4	179.1	109.8
	4	335.7	203.6	269.7
	5	204.5	199.4	202.0
	6	163.4	185.9	174.7

Name		M. M.	Y. S.*	Aver.
Age		12	12	
Weight, Kg.		30.35	30.80	30.58
Phosphoric acid, mg.				
Before:	1	38.4	41.6	40.0
	2	31.8	35.8	33.8
	3	31.2	36.4	33.8
After:	1	52.7	85.2	69.0
	2	29.9	50.7	40.3
	3	15.0	32.5	23.8
	4	44.2	41.6	42.9
	5	25.4	42.3	33.9
	6	34.5	45.5	40.0
Creatinine, mg.				
Before:	1	5.0	5.8	5.4
	2	4.6	5.6	5.1
	3	4.6	5.2	4.9
After:	1	4.0	4.6	4.3
	2	4.3	5.6	5.0
	3	...	5.8	...
	4	8.7†	5.6	...
	5	5.6	5.5	5.6
	6	4.8	5.4	5.1
Ammonia, mg.				
Before:	1	9.3	6.6	8.0
	2	8.6	5.9	7.3
	3	7.6	5.1	6.4
After:	1	8.4	6.9	7.7
	2	5.9	5.8	5.9
	3	5.1	9.3	7.2
	4	13.5	9.7	11.6
	5	8.4	10.1	9.3
	6	9.7	8.0	8.9
Temperature, C.				
Before:	1	36.8	36.6	36.7
	2	36.9	36.5	36.7
After:	1	36.0	36.1	36.1
	2	36.5	36.1	36.3
	3	37.0	36.6	36.8
	4	36.4	37.0	36.7
	5	36.8	36.9	36.9

* The winner's time was six minutes and thirty seconds.
† Because of the small amount of urine excreted, only the total amount for the third and fourth periods is given.

The reaction was determined by means of litmus paper. The various constituents were determined as follows: protein by the boiling method with sulphosalicylic acid; dextrose by Haines' method; total nitrogen by Kjeldahl's method; creatine, creatinine and ammonia by Folin's method, and phosphoric acid by Neumann's method.

RESULTS

Albuminuria.—Although there is some trace of protein in normal urine, the term albuminuria is applied only in cases in which albumin is present in excess. In 1878 von Leube [1] demonstrated experimentally

1. von Leube: Virchows Arch. f. path. Anat. **72**:145, 1878.

for the first time that muscular work results in albuminuria. Since then numerous reports have been published on this subject.

In our experiments, albuminuria was observed following a long distance race in the majority of the boys (93.4 per cent), but it was noted after a short distance race in only two. Quantitatively albuminuria was seen to be highest following the long distance races at the athletic contest, probably as a result of psychic factors. The reason albuminuria was observed even after a short distance race in two fifth grade boys may be attributable to the fact that they took part in a long distance race which was held in the forenoon as well as in a short distance race in the afternoon.

Glycosuria.—The presence of dextrose in the urine was not observed after either a short distance or a long distance race.

Acidity.—As regards the acidity of urine after exercise, Fukusima [2] and Takasaki [3] insisted that there is an increase of acidity, but Nakadate [4] reported that exercise does not always increase the acidity. In our experiments no change in the acidity was noticed after a short distance race, but after a long distance race it was noticeable.

Volume.—In Ranke's [5] experiments on dogs the urine decreased during and soon after the development of tetanus of the leg muscle, and later it increased greatly. Zuntz and Schumburg [6] reported that soldiers showed a great increase in the amount of urine excreted after a march. Recently Minko Dobreff [7] stated that: (1) during and soon after hard muscular work there is a severe but not a long-persisting repression of urine; (2) light muscular work of short duration has no effect on urination, and (3) during the first five minutes after the beginning of hard muscular work there is a great increase in the volume of urine, and then an intense repression occurs.

From our results we cannot draw any definite conclusions; in some cases there was an increase in the volume of urine and in some a decrease during the first thirty minutes after a long distance race, but thereafter there was usually a decrease.

Total Nitrogen Content.—There are many reports regarding the increase or decrease of the total nitrogen content after muscular work.

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2. Fukusima, Kaneko and Tatara: Eiseigaku-Densenbyogaku-Zassi, vol. 16, p. 15.

3. Takasaki: Igaku-Tyuo-Zassi, vol. 20, no. 21, p. 1552.

4. Nakadate: Gekko-Eisi, vol. 2, no. 1.

5. Ranke, J.: Die Blutvertheilung und der Thätigkeitswechsel der Organe, Leipzig, W. Engelmann, 1871, vol. 2, pt. 2.

6. Zuntz, N., and Schumburg, H.: Studien zu einer Physiologie des Marsches, Berlin, A. Hirschwald, 1901.

7. Dobreff, M.: Arch. f. d. ges. Physiol. **213**:511, 1926.

Cathcart,[8] Campbell[9] and Garry[10] stated that there is an increase. Shaffer[11] and Kocher[12] insisted that there is no change. Fukusima[2] reported that the content was increased after exercise in four of seven cases and decreased in three, and that, though he could not draw any definite conclusion, he thought that as a rule it increased. Takasaki[3] showed experimentally that the total nitrogen content was less after exercise. Recently Yasuda[13] measured the total nitrogen excreted during two hours after an 800 meter race, but he likewise could not draw any conclusion; in some cases there was an increase and in others, a decrease.

As we could not record exactly the time of urination before and after the races in the athletic contest, we could compute only the ratio of the total urinary volume and its total nitrogen content. In regard to the absolute volume of total nitrogen excreted at thirty minute intervals, we can sum up the results in the second and third experiments, as follows: The total nitrogen content decreased during the first thirty minutes after exercise and then gradually increased until it reached the value noted before exercise. The ratio of the total nitrogen content to the urinary volume decreased during the first thirty minutes after exercise, as did the absolute volume just mentioned and then increased until it exceeded the value obtained before exercise (fig. 1). The fall in the total nitrogen content soon after exercise was shown by all the subjects in the second and third experiments. We called it the negative phase of the total nitrogen content after exercise. Probably it is attributable to the remarkable change in the distribution of blood caused by muscular work—a temporary hindrance of the function of the kidneys due to anemia of abdominal organs. Furthermore, the severer the fatigue, the greater was the extent of the negative phase. The difference in the results reported by many authors, as previously mentioned, in regard to the total nitrogen content after exercise may be due to the difference in time of urination after exercise. The results obtained in our first experiment obviously prove this fact.

Creatine and Creatinine.—Takasaki[3] reported the appearance of creatine and an increase of creatinine in the urine of adults after exercise. Hirao[14] showed experimentally an increase of creatinine.

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8. Cathcart, E. P.: Physiol. Rev. **5**:225, 1925.
9. Campbell, J. A., and Webster, J. A.: Biochem. J. **16**:106, 1922.
10. Garry, R. C.: J. Physiol. **62**:364, 1927.
11. Shaffer, P. A.: Am. J. Physiol. **22**:445, 1908.
12. Kocher, R. A.: Deutsches Arch. f. klin. Med. **115**:82, 1914.
13. Yasuda and Yamakita: Taiku-Kenkyu, vol. 1, no. 2, p. 201.
14. Hirao: Jika-Zassi, no. 242, p. 86.

In our experiments the ratio of the creatinine to the total nitrogen content increased soon after exercise and then gradually decreased until the original value was reached, and the greater the fatigue, the higher the increase and the longer the time required for the restoration of the original value (fig. 2).

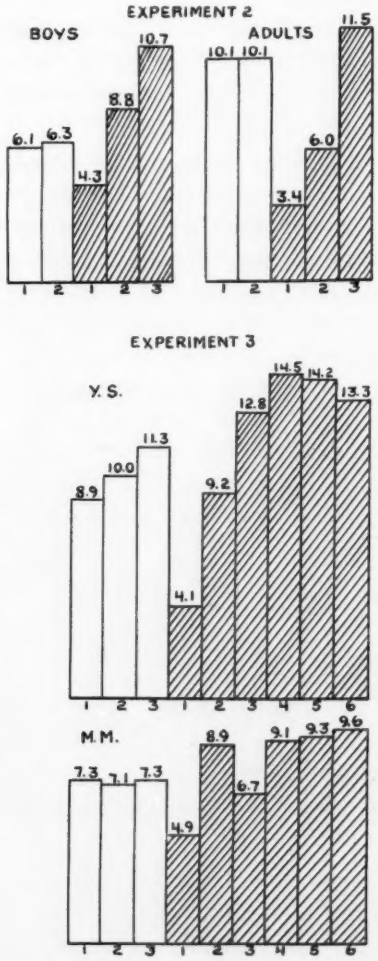

Chart 1.—Graphs showing the ratio of the total nitrogen content to the volume of urine excreted (milligrams of total nitrogen in 1 cc. of urine). In the charts the white columns represent the ratios obtained at thirty minute intervals before a race; the shaded columns, those obtained after a race.

Ammonia.—Although no change was seen in the absolute volume of ammonia per unit of time, the ratio of the ammonia to the total nitrogen content increased after exercise (fig. 3).

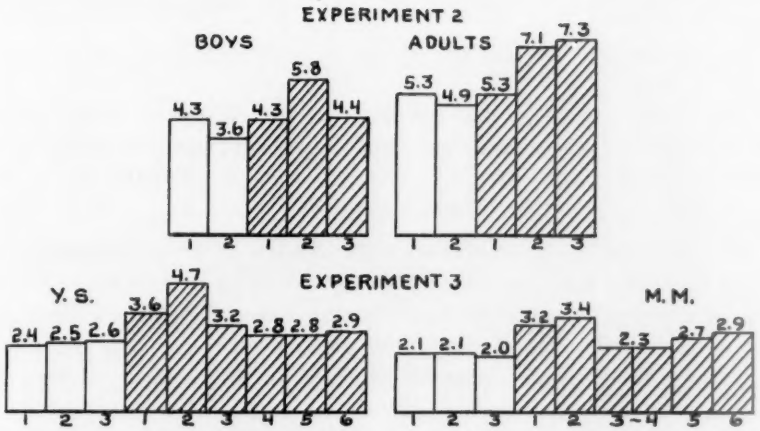

Chart 2.—Graphs showing the ratio of the creatinine to the total nitrogen content (percentage).

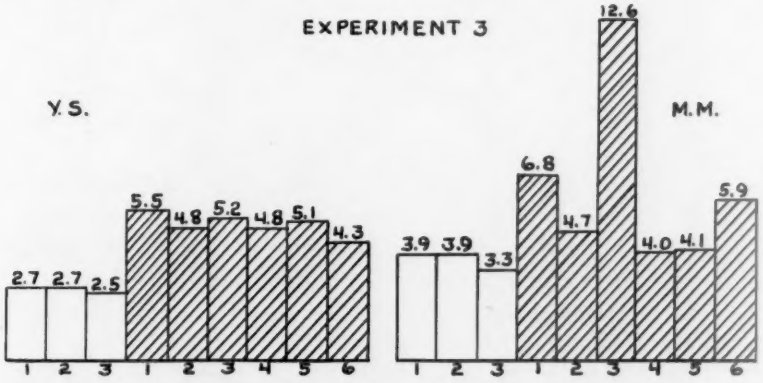

Chart 3.—Graphs showing the ratio of the ammonia to the total nitrogen content (percentage).

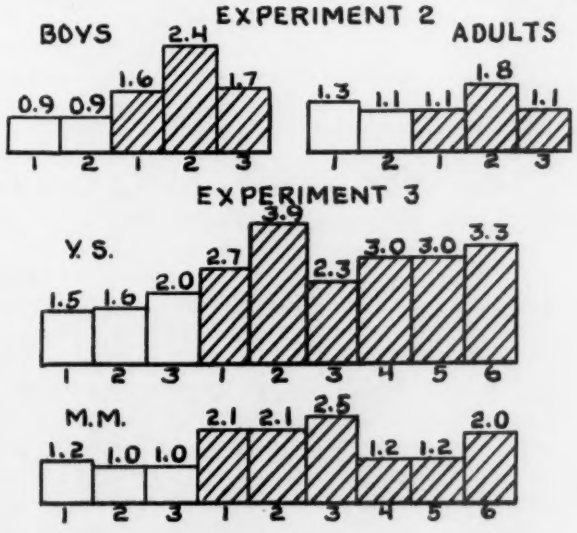

Chart 4.—Graphs showing the ratio of the phosphoric acid content to the volume of urine (milligrams of phosphoric acid in 1 cc. of urine).

Phosphoric Acid.—It was obvious that the phosphoric acid content increased after exercise both per unit of time and per cubic centimeter of urine (fig. 4).

CONCLUSIONS

We observed on three occasions the change of urinary constituents before and after exercise. Thirty-seven boys from 7 to 13 years of age took part in short distance or long distance races. Three men also took part in the race studied in the second experiment.

After a short distance race we observed no albuminuria, no increase of acidity and no remarkable change in the urinary constituents.

After a long distance race albuminuria was present in many cases; the greatest amount of albumin was noted after the races in the contest, probably because of psychic factors. The acidity of the urine was also increased. A remarkable change which was observed was that the total nitrogen content decreased during the period from thirty to sixty minutes after exercise and then gradually rose until it reached normal. The amount of phosphorus increased, but the amount of creatine, creatinine and ammonia was not so significantly influenced by exercise. However, following exercise a rise was seen in the ratio of the total nitrogen content to the volume of urine, the ratio of the phosphoric acid content to the volume of urine, the ratio of the creatinine to the total nitrogen content and the ratio of the ammonia to the total nitrogen content. The ratio of the total nitrogen content to the volume of urine fell only during the first thirty minutes after exercise.

It is obvious that boys become less fatigued during a race than men, as is indicated by the ratio of the creatinine to the total nitrogen content, the time required for the restoration of the creatinine content to a normal level and the extent of the negative phase of total nitrogen excretion.

DICK TEST AND BLOOD AGAR CULTURES AS AIDS IN DIAGNOSIS OF SCARLET FEVER

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During the nine years since its introduction, the Dick test has proved to be a reliable test for susceptibility to scarlet fever. Among about 20,000 persons tested by the Scarlet Fever Committee, none with an original negative reaction to the Dick test has contracted scarlet fever.[1] No nurse at the Cook County Hospital with a negative reaction to the Dick test has contracted scarlet fever, while several whose reactions were positive contracted the disease before they were immunized.[2] At the round table conference on scarlet fever of the American Academy of Pediatrics, held on May 13, 1932, it was brought out that of 953 susceptible nurses immunized to the point of a negative reaction to the Dick test by one of the members none had had scarlet fever, while several nurses who had been incompletely immunized had had the disease.[3]

Confusion of opinion exists, however, in regard to the value of the Dick test in the diagnosis of scarlet fever. The Dicks have repeatedly emphasized that the test is primarily for determining susceptibility and not for the diagnosis of scarlet fever, because of the variable speed with which different persons develop scarlet fever antitoxin during the course of the disease.[4] Many other workers who have studied the

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From the Department of Pediatrics, University of Illinois College of Medicine, the Cook County Contagious Disease Hospital, the Wallace R. Lane Fund of the Scarlet Fever Committee and the John McCormick Institute for Infectious Diseases.

1. Dick, G. F.: Scarlet Fever, with a Consideration of Other Hemolytic Streptococcus Infections, Internat. Clin. **1**:150 (March) 1930.

2. Rhoads, P. S.: Skin Tests and Immunization Against Scarlet Fever and Diphtheria; Results in Nurses of Cook County Hospital, J. A. M. A. **97**:153 (July 18) 1931.

3. Proceedings of the American Academy of Pediatrics, J. Pediat. **1**:778 (Dec.) 1932.

4. Dick, G. F., and Dick, G. H.: Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **82**:265 (Jan. 26) 1924; Results with the Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **84**:1477 (May 16) 1925; The Dick Test, Nations Health **9**:49 (Oct.) 1927; The Control of Scarlet Fever, Am. J. Dis. Child. **38**:384 (Nov.) 1929.

problem have found this conclusion to be true,[5] but there are many others who claim that the Dick test is important in the diagnosis of scarlet fever.[6] Zingher,[7] for example, reported that the Dick test was almost always positive (99 per cent) during the first three days and in 93 per cent of patients during the first five days of the sickness. Schamberg and Kolmer[8] in their textbook stated: "If the test is negative during the first day or two of an exanthem, the individual possesses an antitoxic immunity, and scarlet fever can usually be excluded in the diagnosis." And again: "The Dick test is invariably positive during the first two or three days of scarlet fever." Stimson[9] stated: "The Dick test is positive in the first one to three days in scarlet fever, but usually becomes negative in from six to twelve days." Griffith and Mitchell[10] stated: "The fact that the Dick test is positive in the early days of scarlet fever and becomes negative about the seventh to the tenth day of the disease may be a helpful point in diagnosis."

Many clinicians still use the Dick test in making a diagnosis of scarlet fever and are confused when the reaction is negative during the first few days of the disease or positive later in the course of the disease. The present study was undertaken to obtain further evidence on this point.

METHOD

Between June 20, 1932, and April 7, 1933, 273 white patients admitted to the Cook County Contagious Disease Hospital with a diagnosis of scarlet fever were given a Dick test soon after admission. Exactly 0.1 cc. of standard toxin for the Dick test was injected intradermally into the volar surface of the right forearm and the same amount of the material which had been heated in boiling water for one hour was injected into the left forearm as a control. MacGregor skin test syringes and 26-gage Summit skin test needles, which had been boiled in distilled water, were used. Results were never observed before twenty hours or after twenty-four hours from the time the injections were made. The size and intensity of the reaction were recorded. All

5. Silcock, F. A. E.: The Dick Test at a Fever Hospital, Lancet **2**:1324 (Dec. 26) 1925.

6. Taylor, J. S., and Smith, J.: The Dick Test in Scarlet Fever Patients and in Normal Individuals, J. Hyg. **25**:90 (Feb.) 1926.

7. Zingher, A.: Dick Test in Normal Persons and in Acute and Convalescent Cases of Scarlet Fever, J. A. M. A. **83**:432 (Aug. 9) 1924.

8. Schamberg, J. F., and Kolmer, J. A.: Acute Infectious Diseases, ed 2, Philadelphia, Lea & Febiger, 1928, pp. 354 and 438.

9. Stimson, P. M.: Common Contagious Diseases, Philadelphia, Lea & Febiger, 1932, p. 91.

10. Griffith, J. P. C., and Mitchell, A. G.: Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1927, p. 372.

areas of reaction measuring 10 mm. or more in diameter and of even the faintest degree of pinkness were recorded as indicating a positive reaction. If the reaction to the first test proved to be positive, another Dick test was performed, the tests being repeated every one or two

TABLE 1.—*Results of Dick Test Made After the Onset of Scarlet Fever* *

Day After Onset That Test Was Performed	Number of Patients Tested	Number of Patients Showing Negative Reaction After First Test	Number of Patients Showing Positive Reaction After First Test
1	30	17	13
2	44	28	16
3	45	35	10
4	36	27	9
5	18	14	4
6	18	10	8
7	13	10	3
	204	141 (69.1%)	63 (30.9%)
8	4	3	1
9	7	6	1
10	2	1	1
11	6	4	2
12	4	3	1
13	2	2	0
14	5	5	0
	30	24 (80%)	6 (20%)
15	2	2	0
16	2	2	0
17	2	1	1
18	4	2	2
19	4	4	0
20	2	2	0
21	1	1	0
	17	14 (80.2%)	3 (19.8%)
22	5	5	0
23	2	2	0
24	2	2	0
25	1	4	1
26	4	1	0
27	2	2	1
28	2	0	0
	18	16 (88.8%)	2 (11.2%)
29	1	1	0
30	1	1	0
33	1	2	0
Total.....	273	199 (72.9%)	74 (27.1%)

* Nine cases included here were incorrectly diagnosed as scarlet fever (see tables 2 and 5).

days until a negative reaction was obtained, or, if the results continued to be positive, until the patient left the hospital. Blood agar plate cultures of the nose, throat and surgical lesions, if present, were made for 81 patients. The culture medium, which was prepared by one of us, consisted of 1 cc. of sheep or human blood added to 10 cc. of plain agar for each plate. For the culture from the throat, both tonsils or tonsillar fossae and the nasopharynx were touched with a cotton swab,

and the material obtained was transferred immediately to a plate by rubbing the swab over the whole surface. In taking the cultures from the nose, the swab was inserted at least 1 inch (2.54 cm.) into each nostril and then rubbed over the plate. All of the cultures and the Dick tests were made and observed by us.

COMMENT ON TABLES

Table 1 shows that of the 273 patients who entered the hospital with a diagnosis of scarlet fever, 199 (72.9 per cent) reacted negatively and 74 (27.1 per cent) positively to the first Dick test. A record was kept of the number of days after the onset of the initial symptoms of angina and fever (not the rash) that the first tests were performed. These symptoms were usually first noted either on the same day as the appearance of the rash or on the day preceding it. The incidence of positive reactions decreased and negative reactions increased as more time elapsed. The significant fact is brought out, however, that 56.7 per cent of 30 patients tested on the first day after the onset of scarlet fever showed negative reactions when observed the following day. Of the 44 patients who had their initial tests on the second day after the onset, 63.6 per cent showed a negative reaction the next day. Forty-five patients received their first test on the third day after the onset, and of these, 77.7 per cent gave negative reactions.

Among those receiving their first test at a longer period after the onset, the percentage of negative reactions gradually increased so that of all those whose first tests were made up to one week after the onset, 69.1 per cent showed a negative reaction. Of those who were first tested during the second week of illness, 80 per cent gave a negative reaction; of those first tested during their third week, 80.2 per cent; and of those first tested during the fourth week of illness, 88.8 per cent.

It is, therefore, apparent that the diagnosis of scarlet fever cannot depend on the Dick test made after onset of the disease. The reaction may be negative on the first day of the disease or may be positive later.

On the 74 patients who reacted positively to the first Dick tests, additional tests were made at intervals of one or two days. Table 2 shows that 31 (45.9 per cent) of the 47 patients gave a negative reaction at the end of the first week; an additional 13 at the end of the second week; an additional 9, at the end of the third week; and an additional 2 at the end of the fourth week, making a total of 54 patients who had originally shown a positive reaction and who showed a negative reaction by the end of the fourth week of the disease. A study of the cases in which the Dick tests were persistently positive reveals that 9 of the patients who were admitted with the diagnosis of scarlet fever and whose reaction to the Dick test did not become negative did not

have scarlet fever. This, then, left only 11 patients with scarlet fever of a total of 273 whose reaction to the Dick test did not become negative during their stay in the hospital. Of the group of 54 originally giving positive reactions whose reactions later became negative, 3 did not have

TABLE 2.—*Results of Subsequent Dick Tests on the 74 Patients Who Gave Positive Reactions after the First Test Following the Onset of Scarlet Fever*

Number of Days after Onset that First Test Was Performed	Number of Patients Showing Positive Reactions after First Test	Number of Patients with Originally Positive Reactions Which Became Negative on the Day Indicated
1	13	0
2	16	4
3	10	6
4	9	5
5	4	5
6	8	4
7	3	7
		31 (45.9%)
8	1	1
9	1	3
10	1	1
11	2	1
12	1	4
13	0	0
14	0	3
		44 (59.4%)
15	0	1
16	0	0
17	1	1
18	2	0
19	0	2
20	0	3
21	0	2
		52 (70.2%)
22	0	0
23	0	1
24	0	0
25	1	1
26	0	0
27	1	0
28	0	0
Total.....	74	54 (72.9%)
Number of patients observed throughout hospitalization who never showed a negative reaction. All showed desquamation and other signs of scarlet fever. The average stay in this group was 25.8 days. An average of 3.8 tests were made on each patient.....		11 (14.9%)
Number of patients observed throughout hospitalization who never showed a negative reaction and for whom the final diagnosis was not scarlet fever. The average stay of this group was 13.1 days. An average of 3.4 tests were made on each patient.....		9 (12.2%)
Total.....		74

scarlet fever on admission, but all signs of scarlet fever developed during their stay in the hospital, and their reactions to the Dick test became negative.

Table 3 shows that the total number of patients with scarlet fever who later showed a negative reaction was 253, or 95.8 per cent, of those

tested. We may, therefore, say that although the Dick test cannot be depended on as a test for the diagnosis of scarlet fever, a persistently positive reaction to the test during the whole course of the disease throws great doubt on the correctness of the diagnosis. It does not, however, definitely exclude scarlet fever. The fact that the reaction is

TABLE 3.—*Final Results of the Dick Tests*

	Number of Patients
Patients tested	273
Patients whose final diagnosis was scarlet fever	264
Patients with scarlet fever who showed a negative reaction	253 (95.8%)

TABLE 4.—*Results of Culture on Blood Agar from 81 Patients for Whom the Final Diagnosis Was Scarlet Fever*

	Number of Cases
Both throat and nose cultures positive for hemolytic streptococci	42
Only throat culture positive for hemolytic streptococci	34
Only nose culture positive for hemolytic streptococci	1
Surgical lesions (3 burns, 1 puerperal sepsis) positive for hemolytic streptococci	4
Total	81

Percentage of positive cultures, 100 per cent

TABLE 5.—*Results of Cultures of Blood Agar from 9 Patients for Whom the Final Diagnosis Was Not Scarlet Fever*

Case	Final Diagnosis	Culture
1	Empyema, toxic eruption	Negative
2	Upper respiratory infection	No culture taken
3	Phenobarbital rash	Negative
4	Contact with scarlet fever	Negative
5	Subacute bacterial endocarditis	Negative
6	Lobar pneumonia with toxic flush	Negative
7	Acute tonsillitis	No culture taken
8	Chickenpox	Negative
9	Influenza	Negative

positive at the beginning of the disease and then becomes negative during the course of the disease is great confirmatory evidence that the disease is scarlet fever.

Table 4 gives the results of cultures on blood agar in 81 cases. Our work was begun in order to determine the value of the Dick test in the diagnosis of scarlet fever. As the study progressed, several patients who did not have scarlet fever and whose blood agar plates were negative were encountered. It was then decided to make blood agar plates for all future patients. Of 81 patients from whom cultures were carefully taken, 42 showed positive cultures from both throat and nose, 34, from

the throat alone and 1, from the nose alone. In 4 surgical cases of scarlet fever the cultures from the local lesions were positive. We, therefore, obtained 100 per cent positive cultures in the correctly diagnosed cases of scarlet fever. Of the 9 patients for whom the final diagnosis was not scarlet fever, 7 had negative blood agar plates and from 2 cultures were not taken. These results bring out the great value of the blood agar cultures. A negative culture is strong evidence against the condition of scarlet fever. A positive culture, however, does not prove that the patient has scarlet fever; it simply means that the patient harbors in the throat or nose a Streptococcus haemolyticus that is not identified as a scarlet fever streptococcus. However, in the presence of other clinical findings of scarlet fever, a positive culture confirms the diagnosis. On the other hand, negative nose, throat or wound cultures, properly taken early in the course of the disease, cultured on properly prepared blood agar and properly interpreted, indicate that in all likelihood, the case is not one of scarlet fever.

SUMMARY

1. Two hundred and seventy-three white patients who were admitted to the Cook County Contagious Disease Hospital between June 20, 1932, and April 7, 1933, with a diagnosis of scarlet fever were given a Dick test soon after admission.

2. Of 30 patients tested on the first day of the disease, 17, or 56.7 per cent, showed a negative reaction the next day; and of 204 patients tested at the end of the first week of the disease, 141, or 69.1 per cent, showed a negative reaction.

3. Of the total number of patients who were tested, 264 were discharged with a final diagnosis of scarlet fever and 253 of these, or 95.8 per cent, showed a negative reaction before discharge from the hospital. Eleven, or 4.2 per cent, did not show a negative reaction after an average stay of 25.8 days in the hospital.

4. For 81 patients for whom the final diagnosis was scarlet fever blood agar cultures were made. The hemolytic streptococcus was present in every case.

5. Seven of the 9 patients for whom the final diagnosis was not scarlet fever had negative cultures for the hemolytic streptococcus. Cultures were not made for the other 2 patients.

CONCLUSION

1. The diagnosis of scarlet fever cannot depend on a single Dick test. A persistently positive reaction to the Dick test during the whole course of the disease throws great doubt on the correctness of the diag-

nosis of scarlet fever, while a positive reaction at the beginning of the disease together with a negative reaction during the course of the disease is confirmatory evidence that the disease is scarlet fever.

2. According to our experience, cultures negative for hemolytic streptococci, properly taken at the beginning of the disease on a properly prepared medium, and properly interpreted offer strong evidence against the correctness of a diagnosis of scarlet fever. A positive culture, however, in the presence of the other clinical findings of scarlet fever confirms the diagnosis.

55 East Washington Street.

CALCIUM, PHOSPHORUS AND NITROGEN RETENTION OF CHILDREN

EFFECTS OF ACID-FORMING AND BASE-FORMING DIETS

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This investigation was planned to study the effect of acid-forming and base-forming diets on the metabolism of calcium, phosphorus and nitrogen in growing children. The importance of obtaining more knowledge on this subject is obvious.

A series [1] of experiments on dogs had been instituted in this laboratory in the hope of establishing the effect of the metabolic reaction of the diet on the development of the bones and teeth. Synthetic diets of the Cowgill type were used, and young animals were reared from the time of weaning on similar diets made acid, neutral or basic by the addition of ammonium chloride or of sodium carbonate. Vitamin D was given or withheld in comparable cases in all of the groups. In this series of experiments, the results obtained by roentgenography, blood analyses, the calcium and phosphorus retention tests and the analyses of the bones and teeth indicated that a diet of nearly neutral reaction favors normal development. After the neutral diet, the alkaline was most favorable, and the acid diet was least favorable. When vitamin D, in the form of cod liver oil, was given, nearly all of the unfavorable effects of the acid and alkaline diets disappeared.

A similar comparison of the effects of acid-forming and base-forming diets, but of a considerably more limited extent, with children used as subjects, appeared worth while. Natural diets had to be used, however, and the administration of cod liver oil was omitted since all of the children were outdoors much of the time. The experiment was carried out during the sunny spring months, when it seemed probable that an adequate supply of ultraviolet rays was available at all times.

This work was done from 1927 to 1930.

From the Child Welfare Institute and the Laboratory of Household Science of the University of California.

The problem was suggested and the work directed by Dr. Agnes Fay Morgan, Professor of Household Science of the University of California. Assistance was also given by Dr. Harold E. Jones and Dr. Herbert Stolz of the Child Welfare Institute, and by other members of the staff of the Institute.

1. Morgan, A. F.: The Effect of Acid, Neutral, and Basic Diets Upon the Calcium and Phosphorus Metabolism of Dogs, University of California Publications in Physiology, Berkeley, Calif., University of California, 1934, vol. 8, p. 61.

EXPERIMENTAL DATA

Twelve children, four boys and eight girls, between the ages of 7 and 12 years, from the Fred Finch Orphanage in Oakland, Calif., gave their enthusiastic cooperation as subjects in this study. In table 1 are presented the dates of the periods during which the diets were given, the reactions of the diets and the sex, the number and the average age of the subjects in each group receiving a specific diet.

The chief variable factor in this experimental investigation, that of the potential acidity or basicity of the diet, was furnished by variations in the amounts of

TABLE 1.—*Sex, Number and Average Age of the Group of Children on Each of the Three Acid-Forming and Three Base-Forming Diets.*

Period	Diet	Reaction of Diet	Subjects		
			Sex	Number on Each Diet	Average Age
March 10-17	D	Basic	Girls	5	9.4
April 10-17	F	Basic	Boys	4	7.9
May 3-10	H	Basic	Girls	8	9.8
March 21-29	E	Acid	Boys	4	8.0
March 21-29	E	Acid	Girls	2	9.6
April 22-29	G	Acid	Boys	4	8.0
May 14-21	I	Acid	Girls	8	9.8

TABLE 2.—*Composition of the Daily Intake for Each of the Three Basic and the Three Acid Diets.**

Food	Basic Diet D	Basic Diet F	Basic Diet H	Acid Diet E	Acid Diet G	Acid Diet I
Milk	600	557	600	500	500	500
Meat	100	100	100	100	100	100
Eggs	25	25	25	50	50	50
Butter	50	50	50	50	50	50
Lima bean bread	100	100	100			
Whole wheat bread	...	...	...	140	140	140
Oatmeal	...	...	...	40	40	40
Rice	25	25	25	80	80	80
Potatoes	200	200	200			
Lettuce	100	100	100	50	50	50
Cabbage	...	...	...	110	110	110
Spinach	200	200	200			
Raisins	50	50	50			
Sugar	50	50	50	50	50	50
Total calories	2,334	2,304	2,334	2,181	2,181	2.181

* The amounts of each food are given in grams.

similar natural foods. These foods included cow's milk, chopped beef, eggs, cereals, leafy vegetables, butter and sugar (table 2). The diets were designed to contain an adequate number of calories, an adequate amount and kind of protein and 1 Gm. daily of both calcium and phosphorus as calculated from published tables. The acidity and basicity were calculated from the original values of Sherman and Gettler,[2] and these figures were later checked with the results obtained from actual analyses.

2. Sherman, H. C., and Gettler, O.: The Balance of Acid-Forming and Base-Forming Elements in Foods and Its Relation to Ammonia Metabolism, J. Biol. Chem. **11**:323, 1912.

The diets were fed during eight day periods, with intervals of three or four days between these periods. On each day of the diet periods a definite percentage by weight of the food to be given the children was reserved. All of these samples of the foods comprising one diet were combined, dried to constant weight, ground and stored for analysis.

Determinations of the nitrogen, potassium, sodium and sulphur contents of the samples of dried food were made by the following methods: For the determination of nitrogen, the Kjeldahl method; for that of potassium and sodium the classic Lindo-Gladding procedure;[3] as a check on the determination of sodium, the uranyl zinc sodium acetate method,[4] and for the determination of sulphur, Folin's method as described by Hawk and Bergeim.[5]

For the determination of the contents of calcium, phosphorus, magnesium and chlorine, aliquot samples of a solution of the ash of the diet were analyzed by the following methods: For the estimation of calcium, McCrudden's method;[6] for that of phosphorus, Fiske and Subbarow's method;[7] for that of magnesium Stolba's method, described by Tisdall and Kramer,[8] and for that of chlorine, Volhard and Harvey's method.[9]

Excreta were collected on the last six days of each of the eight day diet periods. The feces of each subject were dried to constant weight, and samples were analyzed for the determination of the nitrogen content by Kjeldahl's method. Aliquot samples of a solution of the ash of the feces were analyzed for their calcium content by the McCrudden method[6] and for their phosphorus content by the Fiske and Subbarow method.[7] The total amount of urine excreted daily was measured and thoroughly mixed, and aliquot samples were taken for analysis. Each morning, samples were tested for p_H by comparison with the colorimetric standards prepared by Michaelis' method.[10] The six daily measured samples were preserved with toluene, combined and analyzed for calcium by the McCrudden method,[6] for phosphorus by the Fiske and Subbarow method[7] and for nitrogen by the Kjeldahl method.

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6. McCrudden, F. H.: The Quantitative Separation of Calcium and Magnesium in the Presence of Phosphates and Small Amounts of Iron, Devised Especially for the Analysis of Foods, Urine and Feces, J. Biol. Chem. **10**:187, 1911.

7. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

8. Tisdall, F. F., and Kramer, B.: Methods for the Direct Quantitative Determination of Sodium, Potassium, Calcium and Magnesium in Urine and Stools, J. Biol. Chem. **48**:8, 1921.

9. Harvey, S. C.: The Quantitative Determination of the Chlorides in the Urine, Arch. Int. Med. **6**:12 (July) 1910.

10. Michaelis, L., and Gyemant, A.: Die Bestimmung der Wasserstoffzahl durch Indicatoren, Biochem. Ztschr. **109**:165, 1920. Kruger, R.: Weitere Ausarbeitung der Indikatorenmethode ohne Puffer, ibid., **119**:307, 1921.

TABLE 3.—*Elementary Composition and Reaction of the Daily Diets*

	Calcium		Magnesium		Potassium		Sodium		Phosphorus		Chloride		Sulphur		Nitrogen		Reaction of Dried Food				Daily Intake of Dried Food, Gm.
																	Cc. Excess Normal Base		Cc. Excess Normal Acid		
	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Dried Food, per Cent	Intake per Day, Gm.	Per Day	Per 100 Gm.	Per Day	Per 100 Gm.	
Basic diet D.....	0.39	1.32	0.06	0.20	1.36	4.57	0.93	3.12	0.38	1.29	0.80	2.69	0.23	0.77	3.50	11.76	129.0	38.4	....	....	336.2
Basic diet F.....	0.44	1.21	0.06	0.16	1.40	3.84	0.76	2.08	0.33	0.91	0.87	2.38	0.22	0.61	3.66	9.96	99.0	36.4	....	....	273.9
Basic diet H.....	0.42	1.38	0.07	0.23	1.33	4.37	0.90	2.95	0.34	1.12	0.85	2.79	0.28	0.91	3.94	12.93	120.0	36.7	....	....	327.5
Acid diet E.....	0.30	1.07	0.06	0.22	0.56	2.00	0.59	2.10	0.36	1.29	0.96	3.44	0.31	1.11	3.95	14.10	....	....	34.8	9.6	356.8
Acid diet G.....	0.30	1.12	0.07	0.26	0.60	2.23	0.60	2.23	0.38	1.42	1.00	3.72	0.32	1.19	3.49	13.00	....	....	38.4	10.3	372.5
Acid diet I.....	0.30	1.14	0.06	0.23	0.76	2.87	0.60	2.27	0.40	1.52	0.89	3.37	0.36	1.36	3.79	14.36	....	....	29.4	7.8	378.7

RESULTS

The exact basicity or acidity of the diets was calculated from a chemical analysis carried out according to Sherman and Gettler's method [2] The chemical composition and the reaction of the daily diets are stated in table 3. It is evident that, although they varied in degree, the basic diets D, F and H and the acid diets E, G and I were actually basic and acid in their respective reactions. The results obtained in the determi-

TABLE 4.—*Average p_H of the Daily Specimens of Urine of Each Subject*

Subject	Basic Diet			Acid Diet		
	D	F	H	E	G	I
Je	7.2	...	7.5	...	...	5.5
G	7.1	...	7.3	...	...	5.6
D	7.2	...	7.4	...	...	5.8
C	7.2	...	7.4	5.3	...	5.8
Ev	7.2	...	7.5	5.2	...	5.5
A	...	...	7.5	...	...	5.4
V	...	...	7.5	...	...	6.0
Et	...	...	7.5	...	...	5.9
W	...	7.2	...	5.3	5.4	...
F	...	7.3	...	5.2	5.7	...
J	...	7.3	...	5.5	5.5	...
B	...	7.3	...	5.4	5.7	...

TABLE 5.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet D* *

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
G	30	9.7	44	28	2	30	14	43	12	19	31	12	414	34	276	310	104
Ev	32	8.5	41	21	2	23	18	40	9	17	26	14	396	38	221	259	137
Ge	28	10.5	48	37	1	38	10	46	22	14	36	10	459	45	242	287	172
D	26	8.2	43	30	3	33	10	49	11	22	33	16	486	52	271	323	163
C	34	10.2	39	24	1	25	14	38	9	16	25	13	381	32	233	265	116
Average values for all subjects			43	28	2	30	13	43	12	18	30	13	427	40	248	289	138

* Expressed in milligrams per kilogram of body weight.

nations of the p_H of the daily specimens of urine of the children while given the various diets are presented in table 4. This table shows that the urine of the subjects on diets D, F and H was more alkaline and had a higher p_H, between 7.1 and 7.5, than that obtained from subjects on the acid diets E, G and I, the p_H of which was from 5.2 to 6.

The calcium, phosphorus and nitrogen balances of the subjects on each of the diets and the average balances for each diet are recorded in terms of milligrams per kilogram of body weight in tables 5, 6, 7, 8, 9 and 10. The data obtained for subjects on the same diet show

11. Footnote deleted by the author.

few wide variations in the intake, the output or the balance of these substances per kilogram of body weight. A summary of the average intake and retention of each element per day, expressed in milligrams, and the calcium-phosphorus ratio of the intake and of the retention with each diet are presented in table 11. The average retention of calcium, expressed in milligrams was the same (14 mg.) with both the acid and

TABLE 6.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet F* *

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
W	25	8.6	47	33	2	35	12	35	9	25	34	1	516	52	323	375	140
F	25	8.0	48	30	3	33	15	36	15	21	36	0	523	52	287	339	184
J	21	8.0	42	23	2	25	17	32	10	22	32	0	410	31	297	328	82
B	23	7.0	51	36	3	39	12	38	14	25	39	−1	553	47	349	396	157
Average values			47	31	2	33	14	35	12	23	35	0	500	45	314	359	141

* Expressed in milligrams per kilogram of body weight.

TABLE 7.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet H* *

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
C	34	10.7	40	19	2	21	19	32	7	11	18	14	374	32	159	181	193
Ev	33	9.0	41	23	3	26	15	33	11	15	26	7	388	34	193	227	161
Je	28	10.7	47	30	1	31	16	37	12	12	24	13	447	28	272	300	147
V	32	9.7	43	21	2	23	20	34	8	13	21	13	397	28	160	188	209
Et	38	9.7	36	18	2	20	16	29	7	16	23	6	338	27	200	227	111
D	28	8.5	48	26	6	32	16	39	9	17	26	13	449	37	246	283	166
A	26	9.5	52	36	2	38	14	42	13	23	36	6	483	45	281	326	157
G	30	10.7	45	27	3	30	15	36	12	17	29	7	424	36	244	280	144
Average values			44	25	3	28	16	35	10	16	26	10	411	33	219	252	159

* Expressed in milligrams per kilogram of body weight.

the basic diets, even though the intake of calcium with the basic diets was 4 mg. higher than that with the acid diets. The average retention of phosphorus was 6 mg. higher with the acid diets (14 mg.) than with the basic diets (8 mg.), but the average intake of phosphorus with the acid diets was nearly one-third greater (51 mg.) than that with the basic diets (38 mg.). In a subject on diet F, the most basic in reaction, was noted the only failure of retention, that of phosphorus, but with the same diet the retention of calcium in this child was that of the

average subject (14 mg.). The average retention of nitrogen, however, was higher (146 mg.) during the basic than during the acid periods (32 mg.), although the average intake of nitrogen with the acid diets (460 mg.) was higher than that with the basic diets (446 mg.).

Table 12 presents the usual findings in respect to the avenues of excretion of the three elements. 1. The output of calcium through the

TABLE 8.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet E* **

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
W	25	8.5	42	26	6	32	10	50	17	14	31	19	423	39	341	380	43
F	24	8.2	44	26	4	30	14	52	17	15	32	20	439	40	383	423	16
J	21	8.2	51	28	6	34	17	62	19	16	35	27	517	42	400	442	75
B	24	7.2	45	27	8	35	10	50	16	17	33	17	456	35	388	423	33
C	34	10.5	32	16	6	22	10	38	8	13	21	17	318	23	281	304	14
Ev	32	8.7	33	16	7	23	10	40	12	13	25	15	334	26	290	326	8
Average values			41	23	6	29	12	49	15	15	30	19	414	34	347	381	33

* Expressed in milligrams per kilogram of body weight.

TABLE 9.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet G* **

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
W	25	8.5	44	19	5	24	20	56	16	23	39	17	513	33	401	434	79
F	25	8.2	44	21	5	26	18	57	22	23	45	12	520	48	423	471	49
J	21	8.2	40	18	5	23	17	49	15	27	42	7	453	27	413	440	12
B	23	7.2	48	28	6	34	14	60	23	27	50	10	550	55	481	536	14
Average values			44	22	5	27	17	55	19	25	44	11	509	41	429	470	38

* Expressed in milligrams per kilogram of body weight.

feces was larger than that through the urine with the basic diets, though the total output of calcium was approximately the same on the acid-forming and on the base-forming diets.[12] 2. The output of phosphorus[13] and of nitrogen was always larger in the urine than in the

12. Zucker, T. F.: The Relation of Acid-Base Equilibrium in the Body to Excretion of Phosphorus and Calcium, Proc. Soc. Exper. Biol. & Med. **18**:272, 1921.

13. Myers, V. C., and Fine, M. S.: The Relative Importance of the Intestines and Kidneys as Excretory Channels, Proc. Soc. Exper. Biol. & Med. **16**:73, 1919.

TABLE 10.—*Daily Calcium, Phosphorus and Nitrogen Balances of Children on Diet I* *

Subject	Weight, Kg.	Age, Years	Calcium					Phosphorus					Nitrogen				
			Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.	Intake, Mg.	Output, Mg.			Balance, Mg.
				In Feces	In Urine	Total			In Feces	In Urine	Total			In Feces	In Urine	Total	
C	34	10.7	33	12	7	19	14	44	11	25	36	8	415	27	415	422	—27
Ev	33	9.0	34	13	8	21	13	46	12	24	36	19	431	27	278	305	126
Je	28	10.7	39	22	3	25	14	52	16	24	40	12	497	34	485	519	—22
V	32	9.7	35	15	3	28	17	47	12	15	27	20	441	30	308	338	103
Et	38	9.7	30	13	3	16	14	40	11	19	30	10	376	25	318	343	33
D	28	8.5	40	15	8	23	17	52	14	23	37	15	499	38	429	467	32
A	26	9.5	42	24	5	29	13	57	16	26	42	15	537	40	546	586	—49
G	30	10.7	37	15	7	22	15	50	14	25	39	11	471	28	443	471	0
Average values			36	16	5	23	15	49	13	23	36	13	458	31	402	433	25

* Expressed in milligrams per kilogram of body weight.

TABLE 11.—*Summary of the Average of Daily Intakes and Retentions of Calcium, Phosphorus and Nitrogen*

	Calcium			Phosphorus			Nitrogen			Calcium-Phosphorus Ratio	
	Intake, Mg. per Kg.	Retention, Mg. per Kg.	Intake Retained, per Cent	Intake, Mg. per Kg.	Retention, Mg. per Kg.	Intake Retained, per Cent	Intake, Mg. per Kg.	Retention, Mg. per Kg.	Intake Retained, per Cent	Intake	Retention
Basic diet D	43	13	30	43	13	30	427	138	32	1.0	1.0
Basic diet F	47	14	30	35	0	*	500	141	28	1.3	*
Basic diet H	44	16	36	35	10	28	411	159	38	1.2	1.6
Aver. values	44	14	32	38	8	21	446	146	32	1.1	1.3
Acid diet E	41	12	30	49	19	38	414	33	8	0.8	0.6
Acid diet G	44	17	38	55	11	20	509	39	7	0.8	1.5
Acid diet I	36	15	41	49	13	26	458	25	5	0.7	1.1
Aver. values	40	14	36	51	14	28	460	32	7	0.8	1.0

* No determination.

TABLE 12.—*Average Percentages of the Total Output of Calcium, Phosphorus and Nitrogen Excreted in the Feces and in the Urine*

	Calcium, per Cent		Phosphorus, per Cent		Nitrogen, per Cent	
	In Feces	In Urine	In Feces	In Urine	In Feces	In Urine
Basic diet D.....	94.0	6.5	40.1	59.9	13.8	86.2
Basic diet F.....	92.1	7.9	33.9	66.0	12.5	87.5
Basic diet H.....	88.2	11.8	37.7	62.3	13.0	87.0
Average values.....	91.4	8.7	37.2	62.7	13.1	86.9
Acid diet E.....	77.7	22.2	45.0	55.0	8.9	91.1
Acid diet G.....	80.1	19.9	43.0	57.0	8.7	91.3
Acid diet I.....	74.1	25.9	40.1	59.9	7.1	92.9
Average values.....	77.3	22.7	42.7	57.3	8.2	91.8

feces, regardless of the reaction of the diet, but with the base-forming diets there seemed to be slightly less phosphorus excreted through the feces (37.2 per cent) and correspondingly more through the urine (62.7 per cent), as compared with the average amounts excreted through the feces (43.0 per cent) and through the urine (57.3 per cent) with the acid-forming diets. The reverse is true in the case of nitrogen; the average amount excreted through the feces with the basically reacting diets (13.1 per cent) was higher than that with the acid diets (8.2 per cent), and the average amount excreted through the urine was lower with the base-forming diets (86.9 per cent) than that with the acid-forming diets (91.8 per cent). This was probably due to the larger amount of vegetable fiber in the basic diets. The calcium-phosphorus ratio of the feces was higher with the basic diets; this was due entirely to the increase in fecal calcium with the diets of basic reaction, since the fecal phosphorus remained approximately the same with the two types of diet.

COMMENT

The average daily retentions of calcium (14 mg.), of phosphorus (from 8 to 14 mg.) and of nitrogen (from 32 to 146 mg.) compared favorably with those observed in other investigations. Sherman and Hawley,[14] who studied children of similar age, reported retentions of 9 mg. of calcium and 10 mg. of phosphorus. Willard and Blunt [15] observed similar retentions of calcium and phosphorus in young children; in older children, however, although they found similar retentions of phosphorus, the average retention of calcium (27 mg.) was higher. In Burton's study [16] the values for the retention of calcium were determined to be between 1 and 5 mg. and the average retention of phosphorus was 11 mg. Boyd, Drain and Stearns [17] found an average retention value of 17 mg. for calcium and of 14 mg. for phosphorus. For younger children, Porter-Levin [18] reported a calcium retention of 4 mg. and a phosphorus retention of 10 mg. Daniels, Hutton, Knott, Everson and Wright [19] determined the average retention both of calcium

14. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375, 1922.

15. Willard, A. C., and Blunt, K.: A Comparison of Evaporated and Pasteurized Milk as a Source of Calcium and Phosphorus and Nitrogen, J. Biol. Chem. **75**:251, 1927.

16. Burton, B.: The Influence of Cereals upon the Retention of Calcium and Phosphorus in Children and Adults, J. Biol. Chem. **85**:405, 1930.

17. Boyd, J. D.; Drain, C. L., and Stearns, G.: Metabolic Studies of Children with Dental Caries, J. Biol. Chem. **103**:327, 1933.

18. Porter-Levin, T.: Calcium and Phosphorus Metabolism of Normal Pre-School Children, J. Am. Dietet. A. **8**:482, 1933; **9**: 22, 1933.

19. Daniels, A. L.; Hutton, M. K.; Knott, E.; Everson, G., and Wright, O.: The Relation of Milk Ingestion to Calcium Metabolism in Children, Proc. Soc. Exper. Biol. & Med. **30**:1062, 1933.

and of phosphorus by their subjects to be 9 mg. The just mentioned investigators [20] also reported, for normal children of between 3 and 5 years, retentions of calcium of from 3 to 10 mg., of phosphorus of from 6 to 8 mg. and of nitrogen of from 34 to 90 mg.

In the literature concerned with the calcium and the phosphorus metabolism of children, little emphasis has been placed on the effect of the reaction of the diets. Some of the children studied in the investigation made by Sherman and Hawley were within the range of the ages of the children used as subjects in this study. When the reactions of the diets used by Sherman and Hawley were calculated, it was found that some were decidedly acid, some neutral and others basic. In their first series of experiments several of the balances determined for E. C., a girl about 12 years old, may be compared with those found in this investigation. In the three experiments with E. C. as subject, although the first diet was basic and the second and third were acid, the intakes of calcium per kilogram of body weight (from 30 and 31 mg.) and the retentions (13 and 14 mg.) were approximately the same. In this investigation it was determined that Et, a girl 10 years old, when given the acid diet I, had a calcium intake of 30 mg. per kilogram of body weight and a calcium retention of 14 mg., which were similar to those determined for E. C. In these two investigations the percentage of the intake of calcium from milk and that from vegetables differed. With the diet which E. C. received, the intake of calcium from milk averaged 92 per cent and that from vegetables 3 per cent, while with the diet given Et, the intake of calcium from milk was only 52 per cent and that from vegetables 25 per cent. This seems to point to a factor other than the food sources of the calcium or the reaction of the diets which influences retention. The reaction of the diet seems, nevertheless, to require consideration, in view of the results obtained in the third experiment of the second series. With the subject E. C. receiving approximately a neutral diet, the intake of calcium per kilogram of body weight was 29 mg. and the calcium retention was 21 mg., about 7 mg. more than the average value obtained in the three experiments of the first series. The percentages of the intake of calcium from milk and from vegetables, however, varied little in the two series.

When given diet H, Et showed a higher retention of calcium than when on other diets. This increase may, however, have been due to slightly higher intake of calcium per kilogram of body weight. E. C., throughout the eight experiments of the second series, when subjected to diets which varied in the reaction, in the intake of calcium per kilogram

20. Daniels, A. L.: Hutton, M. K.; Knott, E.; Everson, G., and Wright, O.: Relation of Ingestion of Milk to Calcium Metabolism in Children, Am. J. Dis. Child. **47**:499 (March) 1934.

of body weight and in the percentage of calcium derived from milk, showed high values for the retention and intake of calcium, regardless of the sources of the calcium or of the reaction of the diet. It is interesting that in the third experiment of that series, with the only neutral diet used by Sherman and Hawley, the retention of calcium in relation to the intake was high, and the retention of the phosphorus had the highest value in the series. In the second experiment of the fourth series of Sherman and Hawley's study, on a basic diet, A. M. had a calcium intake of 50 mg., which was within 1 mg. of that of B (51 mg.) when given basic diet F of the present series. The calcium retention in the case of A. M., however, was one-half that of B, though A. M.'s intake of calcium from milk and from vegetables was 50 and 28 per cent, respectively, and B's intake from these sources, 56 and 25 per cent.

These comparisons suggest support of the hypothesis of Daniels [20] and her co-workers, namely, that the retention of calcium and phosphorus is primarily governed by the physiologic need of the subject rather than by the reaction of the diet, the calcium-phosphorus ratio or the magnitude, or the food source of the intake. It should be noted, however, that in none of the studies of children, other than of rachitic infants, so far reported can the influence of vitamin D be gaged, since there are involved the factors of the varying amounts of exposure to sunshine or to ultraviolet light and of the ingestion of cod liver oil or of viosterol. Parallel experiments on animals [1] seem to indicate that when the amount of vitamin is restricted all of these factors come into play.

In a comparison of the intakes and the retentions with the various diets, in relation to the calcium-phosphorus ratios (table 11), the highest average retention of calcium (16 mg.) and the second highest retention of phosphorus (10 mg.) were obtained with the basic diet H. With this diet, the calcium-phosphorus ratio of the intake was 1.2 and that of the retention, 1.6. The lowest average retention of calcium (12 mg.) and the highest average retention of phosphorus (19 mg.) were obtained with diet E, having an acid reaction. With this diet, the calcium-phosphorus ratio of the intake was 0.8 and that of the retention, 0.6. The basic diet D, with which the calcium-phosphorus ratios of the intake and of the retention were 1, seems to be the only diet in which the intake of each of the three elements was retained in a relatively high percentage.

The outcome appears to be similar to that observed in the parallel, but more protracted, experiments on young dogs.[1] In the latter study the retentions of calcium and phosphorus were similar in dogs given diets of various reactions, provided a sufficiency of vitamin D was given. When the vitamin was not given, however, a definite disadvantage was seen with the acid diets. The nearly neutral diets produced

nearly normal conditions whether the vitamin was given or not. In the study here reported it is assumed that an adequate supply of vitamin D was available from the exposure to sunshine both previous to and at the time of the determinations. In any case, the storage of calcium and of phosphorus is observed to be similar in these normal children subjected to diets of both basic and acid reaction. It is possible that a different state of affairs would appear in the case of rachitic children deprived of vitamin D.

The results of this investigation of the effect of acids and bases on the paths of excretion of calcium and phosphorus are in harmony with those of other studies. Zucker [12] found that when an ordinary diet containing 1.5 Gm. of calcium per day was given, 71 per cent was excreted in the feces and 29 per cent in the urine. With the addition of 300 cc. of tenth-normal hydrochloric acid, 68 per cent of the total calcium was excreted in the feces and 32 per cent in the urine, while with the addition of 15 Gm. of sodium carbonate, 78 per cent was excreted in the feces and 22 per cent in the urine. In all of the determinations, however, the total excretion of calcium in the feces and urine together remained constant. Myers and Fine [13] found that in the adult the ordinary distribution of the excretion of phosphorus was in the proportion of two thirds in the urine and one third in the feces (table 13).

Peters and Van Slyke [21] reported that "few experiments on nitrogen balances of normal children have been made" and that "the amount of nitrogen in excess of that required for endogenous metabolism necessary to promote maximum retention and growth is still to be determined." Wang and her co-workers,[22] in a study of the metabolism of undernourished children of the age of the children in this study, found with an intake of 512 mg. per kilogram of body weight, an output in the feces of 34 mg. and in the urine of 376 mg., or a total output of 410 mg., making a retention balance of 102 mg., or of 20 per cent of the intake. One of the subjects of Ruotsalainen's study [23] had a nitrogen intake of 429 mg. per kilogram of body weight and an output

21. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 1, p. 282.

22. Wang, Chi Che; Kern, R., and Kaucher, M.: Metabolism of Under Nourished Children: IX. A Study of the Basal Metabolism, Caloric Balance and Protein Metabolism During a Period of Gain in Weight, Am. J. Dis. Child. **38:** 478 (Sept.) 1929.

23. Ruotsalainen: Skandinav. Arch. f. Physiol. **41:**33, 1921; quoted in White House Conference on Child Health and Protection: Growth and Development of the Child: III. Nutrition. Report of the Committee on Growth and Development, New York, Century Company, 1932, p. 70, table 4.

in the feces of 86 mg. and in the urine of 313 mg., or a total output of 400 mg. per kilogram. The retention balance of 30 mg. per kilogram in this case was slightly lower than is the average nitrogen retention obtained with the acid diets in this study (32 mg.). The figures obtained in Wang's study are within the range of those of the present study in which with the basic diets there was an average intake of 446 mg. per kilogram and a retention of 146 mg., or 32 per cent of the intake. With the acid diets were recorded an average intake of 460 mg. per kilogram of body weight and a retention of 32 mg., or 7 per cent of the intake.

It is possible that the greater excretion of nitrogen with the acid diets may be due to the formation of ammonia which undoubtedly is necessary for the neutralization of the excess acid. The amount involved, however, 26 per cent of the total intake, is somewhat larger than has hitherto been reported as probably diverted to this purpose. Moreover, these findings seem to indicate that ammonia is not formed merely at the expense of urea but may be produced in addition to the usual metabolic output.

SUMMARY AND CONCLUSIONS

In this investigation of the effects of acid-forming and base-forming diets on the calcium, phosphorus and nitrogen metabolism of children, the diets were proved to be acid and basic both by chemical analysis and by the effect on the urine.

Only with calcium was an outstanding effect of the reaction of the diets obvious in the paths of excretion of the three elements. With the basic diet the excretion of calcium increased in the stool and at the same time decreased in the urine, with the result that the total output of calcium was approximately constant with both acid and basic diets. With the acid diets the percentage of the excretion of phosphorus was only slightly decreased in the stool and correspondingly increased in the urine.

The retention of calcium was uniform and apparently not influenced by the reaction of the diets. The retention of phosphorus tended to be increased with the acid diets, although the considerably larger intake during these periods may explain the apparently larger retention. With only one diet, F, did a really clearcut disadvantage due to the basic reaction appear. If this diet is omitted from consideration, the reaction of the diets may be said to be without effect on the phosphorus balance.

The highest retentions of all of the three elements, calcium, phosphorus and nitrogen, were noted with the basic diets D and H, but the retentions of calcium and phosphorus were equally high with the three acid diets.

A definitely higher retention of nitrogen was observed with the basic than with the acid diets, even though the intakes of nitrogen were slightly larger with the latter. The increase in the excretion of ammonia with the acid diets may account for the difference.

If a disadvantage to children exists in the use of acid diets it appears to lie in the protein rather than in the calcium and phosphorus metabolism.

OLD TUBERCULIN, HUMAN TUBERCLE BACILLUS PROTEIN AND TRICHLORACETIC ACID PRECIPITATE

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MINNEAPOLIS

Extensive experience has identified old tuberculin as one of the most valuable and dependable diagnostic agents used by physicians. The detection of persons who have been infected with tubercle bacilli is so important, however, from the point of view of the clinic and of public health that refinements of tuberculin designed to enhance its specificity and potency are desirable. Seibert's excellent investigations,[1] which resulted in the isolation of the active principle of tuberculin, have made special products available for the Mantoux test, and recently a few reports have appeared in which experiences with the tuberculoprotein precipitated by ammonium sulphate (human tubercle bacillus protein) are recorded. The special object of this paper is to discuss the relative testing merits of three tuberculins, as revealed by my data and those published by other investigators, and also to submit the results of studies of the areas (determined by the area-by-weight method) [2] of the zones of erythema of Mantoux reactions to old tuberculin as compared with responses to tuberculoproteins designated as human tubercle bacillus protein and trichloracetic acid precipitate.

In table 1 are recorded the data obtained in two series of children tested in the outpatient department at the Lymanhurst school. Each child in these two groups received an intracutaneous injection of 0.01 mg. of old tuberculin (Saranac Lake product) into the right forearm. At the same time the 223 patients in the smaller group were tested on the opposite arm with 0.0005 mg. of human tubercle bacillus protein, while the remaining 868 children were tested in a like manner with 0.0005 mg. of the trichoracetic acid precipitate. When readings were made forty-eight hours after the simultaneous application of the two tests, 4 children in the smaller group reacted to old tuberculin but failed

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1. Seibert, F. B.: Am. Rev. Tuberc. **17**:402, 1928; J. Infect. Dis. **5**:383 (Dec.) 1932. Seibert, F. B., and Munday, B.: Am. Rev. Tuberc. **23**:23, 1931; **25**:724, 1932.

2. Stewart, C. A.: Cutaneous Reaction to Tuberculin in Primary Pulmonary Tuberculosis, Am. J. Dis. Child. **45**:1229 (June) 1933; Am. Rev. Tuberc. **28**:844, 1933.

to respond to human tubercle bacillus protein, and 1 child in the larger group was sensitive to human tubercle bacillus protein, but not to old tuberculin. In only five instances, therefore, did the reaction to old tuberculin disagree with that elicited by the tuberculoprotein fractions precipitated by ammonium sulphate or trichloracetic acid. Whether or not the apparent superiority of old tuberculin over human tubercle bacillus protein is of significance will be considered later. When the positive reactions were graded according to their size and severity, a fairly close agreement was found between the responses to old tuberculin and those to human tubercle bacillus protein and the trichloracetic acid precipitate, in that the majority of the reactions fell into the 3 plus class (the lesions had diameters of over 1.5 cm.).

It is interesting to note that of the 1,091 consecutive new patients tested with 0.01 mg. of old tuberculin during 1933 at Lymanhurst

TABLE 1.—*Range of Ages, Number of Patients and Number and Percentage with Positive Reactions to 0.01 Mg. of Old Tuberculin and to 0.0005 Mg. of Human Tubercle Bacillus Protein and Trichloracetic Acid Precipitate* *

Range of Ages, Years	Number of Patients	Number and Percentage† Giving Positive Reactions to	
		O. T., 0.01 Mg.	H. T. B. P., 0.0005 Mg.
1-19	223	31 (13.5)	27 (12.1)
		O. T., 0.01 Mg.	T. P. T., 0.0005 Mg.
1-19	868	116 (13.4)	117 (13.5)
Total	1,091	147 (13.5)	144 (13.2)

* In this and the following tables old tuberculin is indicated by O. T.; human tubercle bacillus protein, by H. T. B. P., and the trichloracetic acid precipitate, by T. P. T.
† The figures in parentheses indicate percentages.

(table 1) only slightly more than 13 per cent gave positive reactions, and retests with 1 mg. of those who gave negative reactions added comparatively few positive responses. About ten years ago more than 30 per cent of the patients tested as a routine at this school gave positive reactions to the Pirquet test. Evidently during the past decade a marked decline has occurred in the incidence of tuberculous infections among the children of Minneapolis who come to Lymanhurst for examinations. Moreover, the percentage of freshmen entering the University of Minnesota who are found to be sensitive to tuberculin has been falling lately. These observations suggest that the declines which are taking place in the incidence of infections and in the death rate due to tuberculosis bear a parallel relationship to one another.

For the purpose of making a more detailed comparative study of the growth in area and the average size of Mantoux reactions to old tuberculin and to two tuberculoprotein precipitates (human tubercle

bacillus protein and the trichloracetic acid precipitate), 200 children of Lymanhurst who were known to be infected were chosen for investigation. Since two tests were to be applied simultaneously in each instance, no children were selected who were exceptionally sensitive to tuberculoprotein. So far as could be determined by repeated clinical and roentgen examinations, the group chosen was comprised exclusively of patients with primary tuberculosis in its more latent stage of fibrosis or calcification. Roentgenograms gave negative results for many of the children but revealed a calcified hilus or enlarged intrathoracic glands or Ghon tubercles in other instances. No child who had demonstrable pulmonary tuberculosis as the result of a reinfection, tuberculosis of the adult type or primary pulmonary tuberculosis in the acute inflammatory stage was included in the group.

In order to obtain distinct reactions of moderate size and also to avoid general febrile responses when two tests were applied simultaneously, 0.02 mg. of old tuberculin and 0.001 mg. of each of the two precipitated materials were selected as suitable doses for intracutaneous injection into the right and left forearms, respectively. The areas of the reactions to those presumably equivalent doses of the different materials used were determined at the end of four successive intervals of twenty-four hours each following the application of the tests, and the results obtained are recorded in table 2. In compiling the data, the 100 children in each group were arranged consecutively with respect to the maximum size attained by the reactions to old tuberculin. The position of each child in his respective series was determined, exclusively, therefore, by his reaction or degree of cutaneous sensitivity to this material. Averages were then calculated for successive and progressively more sensitive groups comprised of 20 patients each, not only for their reactions to old tuberculin injected into the right arm, but for their reactions to the special material injected into the opposite arm.

According to the data in table 2, in each of the two series of children tested the 20 patients who were least sensitive to old tuberculin were those who had the smallest average reaction to human tubercle bacillus protein or the trichloracetic acid precipitate. As will also be seen from an inspection of the data in the table, this parallel relationship between the degree of sensitiveness as indicated by the average size of the two reactions to different materials prevails with one exception (group IV, trichloracetic acid precipitate tests) for the remaining groups of children. In general, therefore, the results obtained by each of the three materials were in fair agreement as to the average relative degree of allergy present in each of the groups tested.

The averages for the first group of 100 patients reveal that 0.02 mg. of old tuberculin and 0.001 mg. of human tubercle bacillus protein produce reactions of nearly equal size. This approximate equality is valid

not only for the mean area of the zone of erythema at successive intervals of twenty-four hours each but for the averages of the maximum sizes which the reaction attained (table 2). Apparently, therefore, the aforementioned amounts of these two preparations are essentially equivalent doses, at least so far as the size of the reaction which each elicits is concerned. According to the data, however, 0.001 mg. of the trichloracetic acid precipitate produces definitely larger epidermal responses on the average (22.6 sq. cm.) than 0.02 mg. of old tuberculin provokes (17.2 sq. cm.). This observation is interpreted as evidence that 0.001 mg. of the trichloracetic acid precipitate is more potent than

TABLE 2.—*Average Area of Mantoux Reactions to Old Tuberculin (0.02 Mg.), to Human Tubercle Bacillus Protein (0.001 Mg.) and to Trichloracetic Acid Precipitate (0.001 Mg.) at Successive Intervals of Twenty-Four Hours, with the Average Maximum Size to Which the Reactions Grew in Two Groups of One Hundred Children*

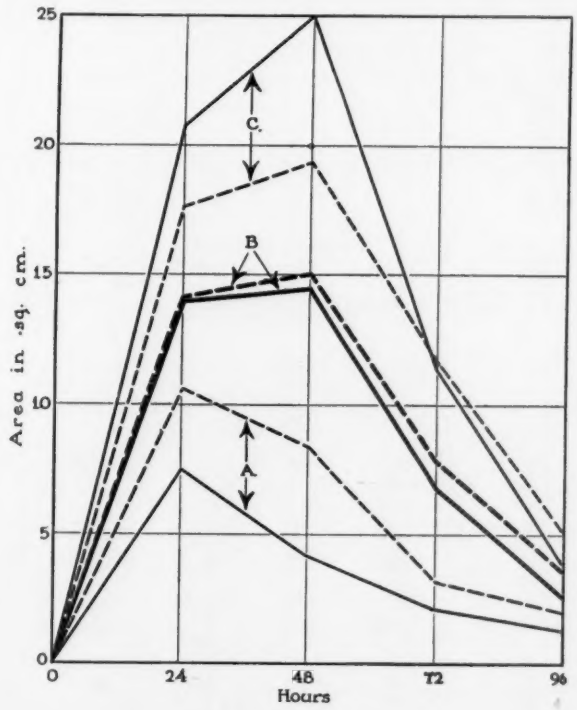
Groups of 20 Patients Each	O. T. Tests, 0.02 Mg. Hours After Test Was Applied When Readings Were Made				H. T. B. P. Tests, 0.001 Mg. Hours After Test Was Applied When Readings Were Made				Average Maximum Size to Which the Reactions Grew	
	24	48	72	96	24	48	72	96	O. T.	H. T. B. P.
	Average Area of the Reactions, Sq. Cm.									
1	3.0	1.4	1.1	0.8	7.5	2.8	2.1	1.1	3.0	7.6
2	9.4	5.4	2.2	1.9	11.5	10.5	3.9	1.8	9.6	15.3
3	15.5	11.3	3.5	1.5	15.2	16.0	8.0	4.3	15.0	18.8
4	18.9	14.8	9.1	5.0	18.8	19.9	11.7	6.3	23.1	23.7
5	25.2	39.3	17.6	3.8	17.5	26.4	13.4	4.4	40.8	28.0
Average	14.0	14.5	6.8	2.5	14.1	15.0	7.8	3.6	18.3	18.6
	O. T. Tests, 0.02 Mg.				T. P. T., 0.001 mg.				O. T.	T. P. T.
1	4.3	1.8	1.4	1.0	9.0	5.9	2.5	1.5	4.1	8.8
2	9.7	6.4	3.2	1.5	15.3	13.8	5.6	2.2	10.6	17.2
3	14.2	8.5	3.0	2.1	22.7	23.9	4.3	3.4	14.9	27.0
4	15.7	18.2	13.1	4.0	15.6	22.0	16.3	8.2	20.7	25.2
5	23.8	29.7	13.8	4.6	21.2	32.1	21.3	5.3	35.9	34.1
Average	13.7	13.3	6.9	2.9	14.9	19.9	11.1	4.1	17.2	22.6

0.02 and 0.001 mg. of old tuberculin and human tubercle bacillus protein, respectively.

The general similarity of the reactions to the three preparations used becomes apparent when one considers the characteristics of the growth in the area of the fields of erythema. Regardless of which material is employed, the positive reactions tend to attain full growth earlier in children who are moderately sensitive than in patients who are markedly allergic to tuberculoprotein. The manner in which the positive reactions to old tuberculin and to human tubercle bacillus protein changed at twenty-four hour intervals and the parallel similarity of these changes throughout the periods of increment and decline of the responses are represented graphically in the chart. The curves (*B*) for the group of 100 patients show how closely the averages for the reactions to old

tuberculin coincided on successive days with the averages for the reactions to human tubercle bacillus protein. Curves *A* and *C* reveal, however, that the responses to human tubercle bacillus protein averaged within narrower limits than the reactions to old tuberculin did.

The analysis of the results obtained in this study indicates that tuberculoproteins precipitated by ammonium sulphate or trichloracetic acid and old tuberculin elicit reactions in children with primary tuberculosis that are similar in many important respects but unlike in other features.



Curves showing the area of Mantoux reactions at twenty-four hour intervals after the simultaneous injection of 0.1 cc. of 1:5,000 old tuberculin and 0.1 cc. of human tubercle bacillus protein. The average of 50 smaller reactions is indicated by *A;* the entire group of 100 cases, by *B,* and the 50 larger reactions, by *C.* The unbroken lines indicate tests with old tuberculin, 0.02 mg. or 0.1 cc. of a 1:5,000 solution being used; the broken lines indicate tests with 0.001 mg. or 0.1 cc. of human tubercle bacillus protein.

A more detailed consideration of the correlation between the reactions to these materials and their dissimilarities is reserved for a communication to be published later, dealing more particularly with the general pattern of the distribution of different degrees of allergy introduced into the child population by tuberculous infections.

TABLE 3.—*Results Obtained by Independent Investigators Following the Use of Human Tubercle Bacillus Protein, Trichloracetic Acid Precipitate and Old Tuberculin in Testing Children and the Significance of the Differences Found as Indicated by Applying the Chi-Square Formula to the Data Obtained* *

Source of Cases	Group	Test Material Used and Dose	Number and Percentage of† Positive Reactions	Number and Percentage of† Negative Reactions	Total	$\sqrt{X^2} = \pm P$	Chances in 100 for the Difference to Arise by Sampling
Data for Children Examined by Stewart [2]							
Lymanhurst	A	O. T., 0.01 mg.	31a (13.5)	192b	223 (a + b)		
		H. T. B. P., 0.0005 mg.	27c (12.1)	196d	223 (c + d)		
			58 (a + c)	388 (b + d)	446 (a + b + c + d)	0.56	57.5
Outpatient department	B	O. T., 0.01 mg.	116a (13.4)	752b	868 (a + b)		
		T. P. T., 0.0005 mg.	117c (13.5)	751d	868 (c + d)		
			233 (a + c)	1,503 (b + d)	1,736 (a + b + c + d)	0.07	94.0
	A + B	O. T., 0.01 mg.	147 (13.5)	944	1,091		
		H. T. B. P. or T. P. T., 0.0005 mg.	144 (13.2)	947	1,091		
			291	1,891	2,182	0.19	85.0
Data for Children Examined by Mariette and Fenger [4] (Their Table 2)							
Children from the sanatorium	C	O. T., 0.01 mg.	67 (61.5)	42	109		
		H. T. B. P., 0.0005 mg.	69 (63.3)	40	109		
			136	82	218	0.28	77.9
Children from the general population	D	O. T., 0.01 mg.	47 (6.9)	632	679		
		H. T. B. P., 0.0005 mg.	58 (8.5)	621	679		
			105	1,253	1,358	1.12	26.0
Children from the sanatorium and the general population (combined)	C + D	O. T., 0.01 mg.	114 (14.5)	674	788		
		H. T. B. P., 0.0005 mg.	127 (16.1)	661	788		
			241	1,335	1,576	0.91	36.0

Data for Children Examined by Mariette and Fenger [4] (Their Table 8)								
Children under 14 years from the general population	E	O. T., 0.01 mg.	102	(8.8)	1,095	1,197		
		H. T. B. P., 0.0005 mg.	50	(8.1)	582	632		
			152		1,677	1,829	0.45	65.0
Data from Children Examined by Aronson and Nicholas [5] (Their Table 1)								
White and Negro children under 14 years	F	O. T., 0.01 mg.	150	(19.1)	635	785		
		H. T. B. P., 0.0005 mg.	153	(19.5)	632	785		
			303		1,267	1,570	0.19	85.0
	A, C, D, E and F combined	O. T., 0.01 mg.	397	(13.3)	2,596	2,993		
		H. T. B. P., 0.0005 mg.	357	(14.8)	2,071	2,428		
			754		4,667	5,421	1.50	13.0
Data for Children Examined by Aronson and Nicholas [5] (Their Table 1)								
White and Negro children under 14 years to whom a larger dose was given	G	O. T., 1 mg.	37	(20.6)	138	175		
		H. T. B. P., 0.005 mg.	20	(11.1)	155	175		
			57		293	350	2.5	1.2
White and Negro children under 14 years for whom the dose of H. T. B. P. was increased	H	O. T., 1 mg.	56	(14.7)	325	381		
		H. T. B. P., 0.05 mg.	37	(9.7)	344	381		
			93		669	762	2.1	3.6
Data for Children Examined by Mariette and Fenger [4] (Their Table 3)								
Children from the sanatorium, given two successive tests	I	O. T., first dose, 0.01 mg.; second dose, 0.02 mg.	68	(75.6)	22	90		
		H. T. B. P., first dose, 0.0005 mg.; second dose, 0.001 mg.	70	(77.8)	20	90		
			138		42	180	0.35	72.0
Data for Children Examined by Funk and Huntoon [6] (Their Table 3)								
Children clinically nontuberculous	J	O. T., 0.01 and 0.02 mg.	7	(16.3)	36	43		
		H. T. B. P., 0.0005 and 0.001 mg.	11	(25.6)	32	43		
			18		68	86	1.06	28.9
	I + J		75	(56.4)	58	133		
			81	(60.9)	52	133		
			156		110	266	0.75	45.0

* The letters a, b, c and d inserted after the figures for the Lymanhurst series indicate the application to the Chi-square formula.
† The figures in parentheses indicate percentages.

TABLE 4.—*Results Obtained by Independent Investigators Following the Use of Human Tubercle Bacillus Protein and Old Tuberculin in Testing Adults and the Significance of the Differences Found as Indicated by Applying the Chi-Square Formula to the Data Obtained* *

Source of Cases	Group	Test Material Used and Dose	Number and Percentage of† Positive Reactions	Number and Percentage of† Negative Reactions	Total	$\sqrt{X^2}$	Chances in 100 for the Difference to Arise by Sampling
Data for Adults Examined by Mariette and Fenger [4] (Their Table 2)							
Adult patients from the sanatorium....	K	O. T., 0.01 mg.	248a (72.9)	92b	340 (a + b)		
		H. T. B. P., 0.0005 mg.	282c (82.9)	58d	340 (c + d)		
			530 (a + c)	150 (b + d)	680 (a + b + c + d)	3.1	1.9
Employees from the sanatorium.....	L	O. T., 0.01 mg.	37 (37.0)	63	100		
		H. T. B. P., 0.0005 mg.	42 (42.0)	58	100		
			79	121	200	0.72	47.2
Adults from the general population.....	M	O. T., 0.01 mg.	58 (27.2)	155	213		
		H. T. B. P., 0.0005 mg.	85 (39.9)	128	213		
			143	283	426	2.8	0.5
Adults combined	K, L and M	O. T., 0.01 mg.	343 (52.5)	310	653		
		H. T. B. P., 0.0005 mg.	409 (62.6)	244	653		
			752	554	1,306	3.7	0.0
Data for Adults Examined by Mariette and Fenger [4] (Their Table 8)							
Aged 15 to 39.....	N	O. T., 0.01 mg.	202 (29.0)	495	697		
		H. T. B. P., 0.0005 mg.	93 (38.5)	167	260		
			295	662	957	2.0	4.6
Aged 20 to 39.....	O	O. T., 0.01 mg.	154 (37.3)	259	413		
		H. T. B. P., 0.0005 mg.	64 (44.4)	80	144		
			218	339	557	1.5	13.4
All adults combined (those aged 15 to 19 omitted)	K, L, M and O	O. T., 0.01 mg.	497 (46.6)	569	1,066		
		H. T. B. P., 0.0005 mg.	473 (59.3)	324	797		
			970	893	1,863	5.4	0.0
Data for Adults Examined by Mariette and Fenger [4] (Their Tables 3 and 4)							
Adult patients from the sanatorium and employees given two successive tests	P	O. T., 0.01 and 0.02 mg.	305 (78.0)	86	391		
		H. T. B. P., 0.0005 and 0.001 mg...	351 (89.8)	40	391		
			656	126	782	4.5	0.0
Data for Adults Examined by Funk and Huntoon [6] (Their Table 2)							
Clinically tuberculous patients.....	Q	O. T., 0.01 and 0.02 mg.	185 (90.7)	19	204		
		H. T. B. P., 0.0005 and 0.001 mg. ..	192 (94.1)	12	204		
			377	31	408	1.3	19.4
Clinically nontuberculous patients.....	R	O. T., 0.01 and 0.02 mg.	98 (71.5)	39	137		
		H. T. B. P., 0.0005 and 0.001 mg. ..	112 (81.8)	25	137		
			210	64	274	2.0	4.6
Adults given two doses (combined)..	P, Q and R	O. T., 0.01 and 0.02 mg.	588 (80.3)	144	732		
		H. T. B. P., 0.0005 and 0.001 mg. ..	655 (89.5)	77	732		
			1,243	221	1,464	4.9	0.0

* The letters a, b, c and d inserted after the figures for the Lymanhurst series indicate the application to the Chi-square formula.
† The figures in parentheses indicate percentages.

Inspection of my own data and of those published by other investigators (tables 3 and 4) discloses that Mantoux tests with human tubercle bacillus protein and the trichloracetic acid precipitate yield results that differ to some extent from those obtained by tests comparable with doses of old tuberculin applied simultaneously in a like manner. In order to arrive at an unbiased estimate of the significance of the differences noted, data derived from various independent sources have been arranged in fourfold tables (tables 3 and 4), and the Chi-square values for these observations have been computed by the use of the following formula:

$$X^2 = \frac{(ad - bc)^2 \ (a + b + c + d)}{(a + c) \ (b + d) \ (a + b) \ (c + d)}$$

$\sqrt{X^2}$ equals P, or the chances in 100 for the difference noted to arise by sampling or by chance. By substituting in this formula the data for the 223 children tested simultaneously with 0.0005 mg. of human tubercle bacillus protein and 0.01 mg. of old tuberculin, X^2 is found to equal $\frac{(31 \times 196) - (27 \times 192)^2 \times 446}{58 \times 388 \times 223 \times 223}$. When this equation is solved, the value for $\sqrt{X^2}$ is found to be ± 0.563, which signifies that 57 chances in 100 exist for the apparent 1.4 per cent superiority of old tuberculin over human tubercle bacillus protein to arise by sampling.[3] The high probability that the difference noted between the results obtained by these two materials may be accidental in origin shows the difference to be of no proved significance. Likewise, no significant difference is found between the results obtained with 0.01 mg. of old tuberculin and 0.0005 mg. of trichloracetic acid precipitate (P equals 94 chances in 100, etc.). My experience with these three materials, therefore, failed to reveal any superiority in the dosage used of human tubercle bacillus protein or the trichloracetic precipitate over old tuberculin, or vice versa, with respect to their relative value in detecting infected children present in the group tested.

When the Chi-square formula is applied to the data of Mariette and Fenger [4] and of Aronson and Nicholas [5] for various groups of children (groups C, D, E and F, table 3) tested with 0.01 mg. of old tuberculin and 0.0005 mg. of human tubercle bacillus protein, the chances in 100 that the differences in the results yielded by these two preparations used were accidental (value of P, table 3) range from 26 to 85. The differences noted, therefore, are not significant. On combining my observations with those reported by other investigators (groups A, C, D, E

3. Yule, G. U.: Introduction to the Theory of Statistics, London, Charles Griffin & Co., 1922, p. 385. Dunn, H. L.: Physiol. Rev. **9**:275, 311 and 341, 1929.

4. Mariette, E. S., and Fenger, E. P. K.: Am. Rev. Tuberc. **25**:357, 1932.

5. Aronson, J. D., and Nicholas, R. V.: J. Immunol. **25**:483, 1933.

* The letters a, b, c and d inserted after the figures for the Lymanhurst series indicate the application to the Chi-square formula.
† The figures in parentheses indicate percentages.

and F combined, table 3), 0.0005 mg. of human tubercle bacillus protein detected 1.5 per cent more positive reactors than 0.01 mg. of old tuberculin revealed. Since 13 chances in 100 exist for this small difference to arise by sampling, the slight apparent superiority of human tubercle bacillus protein over old tuberculin cannot be interpreted as being statistically significant. Independent studies are therefore in agreement and justify the conclusion that in small dosage this special tuberculoprotein fraction and old tuberculin are of essentially equal value in detecting the presence of sensitivity to tuberculoprotein in infected children.

Aronson and Nicholas [5] also used larger doses of these two materials, and their data for children (groups G and H, table 3) indicate that 1.0 mg. of old tuberculin gives better results than either 0.005 or 0.05 mg. of human tubercle bacillus protein yields. In these two series of cases, only 1.2 and 3.6 chances in 100 exist that the apparent superiority of old tuberculin over the special preparation is accidental. In these doses, therefore, old tuberculin is significantly superior to human tubercle bacillus protein, at least when the group surveyed is comprised of children.

Mariette and Fenger [4] and Funk and Huntoon [6] applied two successive tests to small groups of children, using 0.01 and 0.02 mg. of old tuberculin and 0.0005 and 0.001 mg. of human tubercle bacillus protein. Their separate and combined experience failed to demonstrate any significant difference in the results obtained when these amounts of the two materials were used ($\pm$ P equals 0.72, 0.28 and 0.45, groups I and J, table 3).

When adults rather than children are tested, and single small doses are used, the ammonium sulphate precipitate (human tubercle bacillus protein) apparently yields significantly more positive reactors than old tuberculin does. The data of Mariette and Fenger [4] showed a significant superiority in favor of human tubercle bacillus protein (0.0005 mg.) over old tuberculin (0.01 mg.) in each group tested except those designated by letters L and O (table 4). The combined data for groups K, L, M and O show 12.7 per cent better results for the special preparation than for old tuberculin, which is significant statistically, since no chances per hundred exist for this difference to be accidental.

Mariette and Fenger [4] and Funk and Huntoon [6] also applied two successive tests to groups of adults, using 0.01 and 0.02 mg. of old tuberculin and 0.0005 and 0.001 mg. of human tubercle bacillus protein (groups P, Q and R, table 4). Their combined data for 732 cases show 9.2 per cent more reactions to human tubercle bacillus protein than to old tuberculin, and statistical analysis of the data identifies this difference as definitely significant. Attention must be called to the fact,

6. Funk, E. H., and Huntoon, F. M.: J. Immunol. **19**:237, 1930.

however, that the observations presented by Funk and Huntoon [6] failed to demonstrate any significant difference between these two tuberculins when the group tested (group Q) was comprised of clinically tuberculous adults.

COMMENT

On the basis of my own observations combined with those published recently by other investigators, it seems apparent that within the range of dosage used to date the fraction of tuberculin precipitated by ammonium sulphate is not significantly superior to old tuberculin so far as efficiency in detecting infected children is concerned. Small amounts of human tubercle bacillus protein, however, elicit positive reactions in significantly more adults than do comparable doses of old tuberculin. This discovery is rather surprising and suggests the existence of a previously unsuspected fundamental difference in cutaneous sensitivity to tuberculoprotein in infected adults as compared with that present in allergic children. The greater prevalence of pulmonary tuberculosis of the reinfection type in the adult groups tested can hardly be advanced as a possible explanation for this peculiar situation, owing to the fact that Funk and Huntoon [6] found no significant difference in the results obtained with old tuberculin and those obtained with human tubercle bacillus protein when these materials were applied to a group of clinically tuberculous adults (group Q, table 4). There remains, however, the possibility that the superiority of human tubercle bacillus protein over old tuberculin may be dependent in part on the size of the protein molecule present in the preparation used, the sensitiveness to tuberculoproteins of different molecular sizes changing as age advances. In a personal communication from Drs. E. R. Long and F. S. Seibert, I am informed that the molecular weight of the tuberculoproteins in different preparations are as follows: human tubercle bacillus protein, 34,000; Seibert's trichloracetic acid precipitate, 8,000; and the new material soon to be available, 3,000. Since infected persons react to each of these preparations, it seems that tuberculous infections induce sensitivity to special proteins the molecular sizes of which may range considerably, and it is possible that, as the allergy wanes with the passing years, sensitivity to the tuberculoprotein fraction of relatively small molecular size disappears before allergy to the large or aggregate protein molecule is lost. An occurrence of this nature probably should explain the positive reaction to human tubercle bacillus protein of certain adults whose response to old tuberculin is negative. This speculation raises questions of interest relative to peculiarities of allergy in adults as compared with those present in infected children and suggests the possibilities of a new line of attack directed toward their solution. The problem probably is

far from being as simple as was outlined earlier and doubtless requires considerable investigation before any positive statements are justified.

Despite the superiority of human tubercle bacillus protein for testing adults when small doses are employed, the use of this material for the discovery of infected adult patients is inadvisable for important reasons. This preparation of tuberculoprotein (as well as the trichloracetic acid precipitation) is a good antigen and apparently possesses the property of rendering human beings [6] and animals [7] sensitive to the material when it is injected into uninfected nonallergic bodies. Its use as a routine may therefore sensitize patients who have not been infected and thereby ruin the significance of subsequent Mantoux tests applied to them.

CONCLUSIONS

This study, with other investigations dealing with the relative merits of old tuberculin and tuberculoproteins (human tubercle bacillus protein and the trichloracetic acid precipitate), apparently justifies the following conclusions:

1. When Mantoux tests are applied to groups comprised of children, using 0.01 and 0.02 mg. of old tuberculin and 0.0005 and 0.001 mg. of the human tubercle bacillus protein trichloracetic acid precipitate, no one of these three materials proves to be significantly superior to the others in detecting the infected allergic persons present in the group. Within this range of dosage these three materials are of equal value when surveys on tests with tuberculin are made on children.

2. When Mantoux tests are applied to groups comprised of adults, 0.0005 and 0.001 mg. of human tubercle bacillus protein yield significantly more positive reactions (about 10 per cent) than do 0.01 and 0.02 mg. of old tuberculin.

3. This difference between children and adults with respect to the incidence of positive reactions to small but presumably equivalent doses of old tuberculin and human tubercle bacillus protein is interpreted as indicative of the existence of a significant fundamental dissimilarity between the cutaneous sensitivity to tuberculoprotein present in children and that in adults.

4. This allergic difference between the two age groups, which presumably develops as time elapses following a tuberculous infection, may be due to a gradual loss of sensitiveness to the smaller protein molecule of old tuberculin and to a longer continuance of allergy to larger aggregate tuberculoprotein molecules such as are present in human tubercle bacillus protein. Additional data must be collected, however, before this theory can be accepted.

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7. Seibert, F. B.: Proc. Soc. Exper. Biol. & Med. **30**:1274, 1933; Nat. Tuberc. A. Tr., 1933, p. 165.

5. For reasons explained in the text, the greater prevalence of pulmonary tuberculosis of the reinfection or of the adult type in the adults as compared with the children tested apparently does not explain the testing superiority in older patients of small doses of human tubercle bacillus protein over equivalent doses of old tuberculin.

6. The averages for the Mantoux tests applied simultaneously on 100 allergic children with primary tuberculosis in its more latent fibrotic or calcified stage and no demonstrable tuberculosis of the reinfection type, 0.02 mg. of old tuberculin and 0.001 mg. of human tubercle bacillus protein being used, disclose the existence of the following similarities between the reactions to the two materials: (*a*) Positive reactions attain full growth earlier in children who are moderately sensitive than in patients who are very allergic to tuberculoprotein. (*b*) The averages for the areas of the reaction to each material are approximately equal at corresponding intervals of twenty-four hours throughout the periods of increment and decline of the response. (*c*) The mean degree of sensitivity to tuberculoprotein present in a group of 100 infected children as expressed in terms of the averages for the maximum sizes to which the reactions grew was found to be practically the same for each material (18.3 sq. cm. for the reactions to old tuberculin and 18.6 sq. cm. for those to human tubercle bacillus protein [table 1]).

7. With respect to the points mentioned earlier, 0.02 mg. of old tuberculin and 0.001 mg. of human tubercle bacillus protein proved to be essentially equivalent doses for skin tests.

8. The absolute range in the area of the reactions to 0.001 mg. of human tubercle bacillus protein was less than that noted for the responses to 0.02 mg. of old tuberculin.

9. When essentially equal doses are used, tuberculoprotein precipitated by ammonium sulphate or trichloracetic acid and old tuberculin produce reactions in infected children that are similar in many respects but are unlike in other features.

10. Since the antigenic properties of human tubercle bacillus protein are such that injections of this material may possibly sensitize uninfected persons to tuberculoprotein, the use of human tubercle bacillus protein for testing children and adults seems inadvisable and probably should be discontinued in favor of efficient preparations known to be practically nonantigenic.

11. A new purified, nonsensitizing, standardized tuberculin containing a tuberculoprotein of low molecular size and containing no protein except that produced by Mycobacterium tuberculosis will soon be available, and no doubt it should and will displace old tuberculin.

12. The data indicate that the incidence of tuberculous infection is falling appreciably in Minnesota at the present time.

HEMOGLOBIN INDEX AND JAUNDICE OF THE NEW-BORN

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To the new-born infant the extra-uterine environment presents many new problems. At birth the rosy complexion of the skin is similar to that of a plethoric person. This rosiness, however, is not caused by polycythemia, but is rather an erythema neonatorum and disappears after a few days, only to be replaced by the yellowness of jaundice.

The most generally accepted explanation of the occurrence of icterus neonatorum is that it accompanies the infant's postnatal readjustment from an environment which required polycythemia for oxygenation to one which does not. Because of the change in environment after birth, hemolysis occurs, which is the direct cause of the hyperbilirubinemia. Since the liver is incapable of excreting all of the increased amount of bile pigment in a normal manner, it passes some of it into the blood stream and jaundice results.

According to our observations, polycythemia is absent in the fetus, the red blood cells increasing in number at the time of labor and as the result of many unknown factors accompanying birth. This increase in the number of red blood cells is followed in turn by a rapid decrease of these cells, but we have been unable to determine the manner in which this increase and decrease occur. On the basis of our experiments we have come to the conclusion that hemolysis occurs in the placenta. Blood counts were made, and the results showed that there were on an average 500,000 more red blood cells in the blood of the umbilical artery than in that of the umbilical vein, leading us to the conclusion that hemolysis is greater in the placenta than it is in the fetus. This fact justifies Lénárt's [1] theory that the reduction in the number of red blood cells precedes the polycythemic state and that the unknown destructive elements reach the blood stream by way of the placenta. In other words, hemolysis occurs and leads to hyperbilirubinemia.

From the Gynecologic and Obstetric Clinic of the University of Francis Josef, Dr. John Berecz, director.

1. Lénárt, G.: Treatment of Icterus Neonatorum, Orvosi hetil. **72**:830 (July 15) 1928.

Ada Hirsch,[2] Ylppö and others [3] have shown that jaundice of the new-born occurs as a result of hyperbilirubinemia: jaundice appears if the amount of bile pigment in the blood passes a certain limit and does not if it remains below this limit. Most investigators attribute the increase of bile pigment and the resulting jaundice to disorders of the liver. If the liver is unable to excrete bile pigment as rapidly as it is produced, jaundice results, but it does not occur if the amount that is excreted equals the amount that is produced.

According to the observations of Heimann [4] a surprising drop in the hemoglobin index is noticed in cases of jaundice. Our explanation for this occurrence is as follows: Hemolysis in the new-born acts as an irritant to the hematopoietic organs, and they respond by producing an increased number of red blood cells. The newly and quickly formed

TABLE 1.—*Average Hemoglobin Indexes for Twenty-Nine New-Born Infants with Jaundice*

Age, days	2	3	4	5	6	7	8
Hemoglobin, percentage	95	97	99	97	94	96	95

TABLE 2.—*Average Hemoglobin Indexes for Twenty-Five Normal Infants*

Age, days	2	3	4	5	6	7	8
Hemoglobin, percentage	104	104	106	104	104	102	96

red blood cells, however, lack the normal amount of hemoglobin, which brings about the drop in the hemoglobin index of the red blood cells even before jaundice occurs. In order to clarify the relationship between the presence of jaundice and the drop in the hemoglobin content we compared the hemoglobin index of twenty-five new-born infants without jaundice to that of twenty-nine new-born infants with jaundice. The average hemoglobin index of those with jaundice is shown in table 1. The average hemoglobin index of those without jaundice is shown in table 2. The skin of four of the twenty-five jaundiced infants was an unusual bluish white, which indicated that the bile pigment content of the blood had not increased. The average hemoglobin indexes for these four infants are shown in table 3.

2. Hirsch, A.: Die physiologische Ikterusbereitschaft des Neugeborenen, Ztschr. f. Kinderh. **9**:196, 1913.

3. Ylppö, A.: Ztschr. f. Kinderh. 1913, vol. 9. Baar, H., and Stransky, E.: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928. de Jeney, A.: Orvosi hetil. **70**:43, 1925.

4. Heimann: Ztschr. f. Geburtsh. u. Gynäk **68**:169, 1911.

According to Ylppö, in the intra-uterine period and in the early postnatal period the amount of bile pigment that is present governs the rate of the secretion of bile, and the occurrence of jaundice is likewise dependent on the amount of bile pigment. According to Volhard [5] the degree of jaundice is dependent on the amount of bile pigment that is present in the blood of the umbilical cord. The amount of bile pigment present in the blood of the cord indicates the intensity of the jaundice. In other words, the lower the bile pigment content in the blood of the cord the greater the secretory activity of the liver, which controls the intensity of the jaundice. According to our observations,

TABLE 3.—*Average Hemoglobin Indexes for Four Jaundiced Infants with Bluish-White Skin*

Age, days	2	3	4	5	6	7	8
Hemoglobin, percentage	111	109	112	105	106	99	98

TABLE 4.—*Blood Examination Made for Ten Infants Delivered by Cesarean Section*

	Age	Red Blood Cells, Thousands	Hemoglobin, Percentage
From umbilical vein and heel	At birth	4,200	79
From the heel	2 hours	4,600	85
	6 hours	5,200	90
	12 hours	4,900	90
	2 days	4,500	92
	3 days	4,800	80
	4 days	4,900	88
	5 days	4,500	73
	6 days	4,400	77
	7 days	4,100	82
	8 days	4,200	80
	9 days	4,100	80
	10 days	4,100	78
	11 days	4,100	76

whether jaundice will or will not occur can be foretold from the hemoglobin index. If the index is less than 100 per cent, jaundice will result; if it is greater, jaundice will not appear.

According to the observations of Adler [6] the bile pigment content of the blood of the umbilical cord in infants delivered by cesarean section is only 0.5 mg. per hundred cubic centimeters, whereas in those born normally it is 1.3 mg.

Because of a lack of necessary means and instruments we were obliged to omit the bilirubin test of the blood plasma and confine our examinations to clinical observations. We made blood counts and

5. Volhard, E.: Ueber die Entstehung des Ikterus der Neugeborenen, Klin. Wchnschr. **9**:1433 (Aug. 2) 1930.

6. Adler, K.: Der Blutzerfall unter der Geburt und in den ersten Lebenstagen (Beitrag zur Pathogenese des Icterus Neonatorum), Arch. f. Gynäk. **144**:586, 1931.

determined the hemoglobin indexes for the infants delivered by cesarean section. Among these ten infants only three were jaundiced. The fact that the hemolysis was so slight in these cases makes it difficult to give an explanation for the presence of jaundice. The number of red blood cells and the hemoglobin index barely rose and dropped. We were unable to attribute the cause to any disorder of the liver since the jaundice disappeared within a few days. The most interesting finding was that the average hemoglobin index was less than 100 per cent.

In the investigations which we are conducting at present in an attempt to determine the cause of icterus neonatorum we started with the following premise: The first hematopoietic organ in the fetus is the area vasculosa in the mesoderm. The hematopoietic function is taken over by the liver, then by the spleen and finally by the bone marrow. In those animals which lack bone marrow (fish), this function remains localized in the spleen. Let it be supposed first that there is a closer connection between the hematopoietic organs and the reticulo-

TABLE 5.—*Average Hemoglobin Indexes for Ten Infants Delivered by Cesarean Section*

Age, days	1	2	3	4	5	6	7	8
Hemoglobin, percentage	94	102	83	90	81	87	100	95

endothelial system in the new-born than in the adult; second, that the reticulo-endothelial system not only forms the bile pigment from the destroyed red blood cells but is capable of removing the partially formed hemoglobin from the hematopoietic organ itself. Our theories, if experimentally substantiated, would show that the reticulo-endothelial system is capable of forming bile pigment not only from the completed hemoglobin but also from that which is incomplete. Our next step is to determine the total hemoglobin content of the blood (hemoglobin index and the total amount of blood) and at the same time to observe how the bilirubin level changes, without, however, there being a decided drop in the total bilirubin content or a rise in the bilirubin level. Our theories, if substantiated, would prove that the reticulo-endothelial system and the hematopoietic organs, although anatomically different, are functionally alike.

SUMMARY

1. The hemoglobin index of the new-born is less than 100 per cent when jaundice occurs, but more than 100 per cent if jaundice does not occur.

2. From the hemoglobin index one can foretell whether or not jaundice will occur.

3. Hemolysis does not necessarily precede jaundice. The formation of bilirubin can be attributed to some as yet unknown histologic function.

PROPHYLAXIS OF SIMPLE ANEMIA IN INFANCY WITH IRON AND COPPER

EFFECT ON HEMOGLOBIN, WEIGHT AND RESISTANCE TO INFECTION

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Interest in the subject of the present study was stimulated on reading Mackay's [1] report on nutritional anemia in infancy. The conclusions reached in that report, if confirmed, would demand that all children during the first year or two of life receive a fairly large daily supplement of iron.

The literature on anemia in infancy has been adequately covered in the aforementioned report, and only additional pertinent contributions will be referred to here. The most intriguing of recent publications are those dealing with the possibility that copper may play a significant rôle in the synthesis of hemoglobin. The results of the experiments of Elvehjem and Hart [2] on animals to the effect that, whereas impure inorganic salts of iron cured nutritional anemia, the pure salts failed to do so, unless supplemented by small amounts of copper, have already been applied by clinicians to the treatment of anemia. The most carefully controlled experiments with infants were those carried out by Josephs [3] in the comparison of a series of cases of anemic infants treated with iron alone with a series in which both copper and iron

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1. Mackay, H. M. M.: Nutritional Anemia in Infancy with Special Reference to Iron Deficiency, Medical Research Council, Spec. Rep. Ser. 157, London, His Majesty's Stationery Office, 1931.

2. Elvehjem, C. A., and Hart, E. B.: Necessity of Copper as Supplement to Iron for Hemoglobin Formation in the Pig, J. Biol. Chem. **95**:363 (Feb.) 1932.

3. Josephs, H.: Treatment of Anaemia of Infancy with Iron and Copper, Bull. Johns Hopkins Hosp. **49**:246 (Oct.) 1931.

were used. He found that in the second series in which copper was used as a supplement, a more rapid rise in the amount of hemoglobin occurred. Lewis [4] and Bloxsom [5] obtained similar results, the latter with infants seen in private practice. Mackay [6] disagreed with Josephs [3]; she found that in cases of nutritional anemia, the response of the infants treated with copper was similar to that of infants treated with iron alone. She concluded that the deficiency in these babies was one of iron, not one of iron and copper. Elvehjem [7] showed that in rats copper is not necessary for the absorption of iron in the liver but is essential for the synthesis of hemoglobin. It is interesting to note that a similar rôle for copper has been suggested in the synthesis of the respiratory pigment, chlorophyl, in plants and trees (Orth, Wickwire and Burge [8]).

It is not yet proved that a deficiency in copper plays a part in ordinary nutritional anemia in the human infant. Gorter [9] and his co-workers showed that in a small series of children with nutritional anemia the copper content of the blood was more than twice that in new-born infants and markedly higher than that in convalescent children used as controls. He explained this, in view of the presence of anemia, as a response to the greater necessity for the production of hemoglobin by the mobilization of copper in the blood. He also stated that there is no evidence that the blood of twins or of premature infants has a lower copper content than that of full term, new-born infants.

OBJECTS AND METHODS OF INVESTIGATION

In this investigation the primary objects were to obtain statistical proofs of (*a*) any condition of ill health resulting from the so-called simple anemia in infancy, and (*b*) any improvement in health and in the resistance to infection obtained by the addition to the diet of an iron salt, either with or without the supplement of copper. We were given the opportunity, through Dr. Daniel Longpré, of pursuing our investigations at the Crèche Youville, a large institution for foundlings.

In our series of 233 infants, the distribution according to ages at the beginning of the study was as follows: One hundred and ten infants were under 2 months of age; 62, from 2 to 5 months; 36, from 5 to 8 months, and 25, over 8 months.

4. Lewis, M. S.: Iron and Copper in the Treatment of Anemia in Children, J. A. M. A. **96**:1135 (April 4) 1933.

5. Bloxsom, A. P.: Copper and Iron Requirements in Infancy, South. M. J. **25**:40 (April) 1932.

6. Mackay, H. M. M.: Copper in Treatment of Nutritional Anaemia in Infancy, Arch. Dis. Childhood **8**:145 (April) 1933.

7. Elvehjem, C. A.: The Action of Copper in Iron Metabolism, J. Biol. Chem. **97**:16 (July) 1932.

8. Orth, O. S.; Wickwire, G. C., and Burge, W. E.: Copper in Relation to Chlorophyl and Hemoglobin Formation, Science **79**:33 (Jan.) 1934.

9. Gorter, E.: Copper and Anemia, Am. J. Dis. Child. **46**:1066 (Nov.) 1933.

Thus, the great majority when first included were less than 5 months old. The average period of observation of each child was nine months; no child who had not been observed for at least three months was included. All of the premature infants were excluded and only the normal babies considered. Each child was examined on its monthly birthday, the weight recorded and the history of infections or of abnormal temperatures obtained from the chart. The infants were placed on a milk diet until they were 3 months old; browned wheat flour was then added to the bottle. Undiluted milk was given early; an infant of 3 months received approximately 20 ounces (590 cc.) daily, and an infant of 6 months, from 30 to 35 ounces (887 to 1,834 cc.). The milk was obtained from the institution's private herd, and a good deal of it was from Jersey cows. Corn-starch was added to the diet of the babies at the age of 5 months, and porridge at the age of 6 months. After the age of 8 months eggs and meat were given them twice a week, and strained vegetables, mostly carrots and potatoes, daily. All of the infants during the period of observation received tomato juice and 2 drops (4,000 international vitamin D units) daily of a concentrated commercial preparation of irradiated ergosterol in oil; at 6 months of age the dose was increased to 3 drops daily. No case of rickets developed with this dosage; if the condition was present before the initiation of the dietary regimen, it was usually cured within a few months. The nutritional requirements of the infants used in our investigation were obviously well fulfilled.

Grouping of Cases According to the Dosage of Iron and Copper.—In dividing the infants into three groups, namely, those used as controls, those receiving iron and those receiving iron and copper, no attempt was made to distribute them according to ages and weights. They were assigned to each group in rotation. The iron salt used was ferric glycerophosphate, which was supplied in a palatable solution, each teaspoonful of which contained 7 grains (0.45 Gm.) of the salt or 1 grain (0.064 Gm.) of metallic iron. The infants in the group receiving copper in addition to iron were given $\frac{1}{96}$ grain (0.67 mg.) of copper sulphate. Chemical analysis of the iron salt showed it to contain but minute traces of copper, amounting to 0.6 mg. per hundred grams. The preparation of iron and ammonium citrate used by Mackay contained almost three times as much copper. The preparation of iron or of copper was administered by diluting it in a little water, or occasionally by adding it to the bottle if the baby refused it by spoon. Both the group receiving iron and that receiving iron and copper were divided in halves, one half of the children in each group receiving the equivalent of $1\frac{1}{2}$ grains (0.096 Gm.) of metallic iron daily and the other, 3 grains (0.19 Gm.). In addition to this amount of iron, those in the group also receiving copper were given either $\frac{1}{32}$ grain (1.34 mg.) of the copper salt daily or, in the case of those receiving the smaller dosage of iron, $\frac{1}{64}$ grain (0.67 mg.). This grouping was made in order to ascertain whether an increase in the amount either of the iron or of the copper in the diet further increases the hemoglobin content. Even when but a few days old, the infants tolerated the preparations well, provided the size of the dose was made very small at the beginning and increased gradually.

Estimations of Hemoglobin.—The Sahli hemoglobinometer was used for all estimations. On the Sahli scale, 100 per cent represents 17.2 Gm. of hemoglobin per hundred cubic centimeters of blood. Our hemometer was standardized at intervals of six months by the Van Slyke oxygen capacity method. All readings were made by the same person.

Although the majority of the readings were made in the morning, a small number were scattered throughout the day. It was thought, therefore, that a

determination of the daily variations, if any, in the hemoglobin curve should be made in order that any necessary correction might be applied. For this purpose 7 healthy infants, between the ages of 4 and 7 months, were chosen from another institution. These infants had been almost entirely free from infections and were living under excellent conditions of care and diet. Estimations of hemoglobin were made every two hours for a period of two days, and the individual variations are recorded in table 1. In chart 1 are shown hemoglobin curves for 3 children, the one with the highest level of hemoglobin, the one with the lowest and one with a level about midway between the other two. From these curves, it is to be noted that the variations in the hemoglobin value in the individual cases were slight, and, in the majority of instances, within the probable error of reading. No set of figures in the literature [10] for the variations in the hemoglobin content showed as slight a difference as these for a two day period.

The percentages of hemoglobin for the 69 children comprising the control group were averaged by the following method, which is that used in the calculations of the percentages for all of the other groups. For any one month, two averages were calculated, one the average percentage of hemoglobin in the children from

TABLE 1.—*Variations in the Percentage of Hemoglobin in Seven Infants Over a Two Day Period*

Infant	8 a.m.	10 a.m.	12 M.	2 p.m.	4 p.m.	6 p.m.	8 a.m.	10 a.m.	12 M.	2 p.m.	4 p.m.	6 p.m.
1	60	59	62	62	59	61	57	61	60	57	59	62
2	68	66	68	67	69	67	67	69	69	72	73	67
3	66	60	58	57	66	63	66	61	64	60	65	64
4	76	71	66	77	72	68	68	71	70	71	68	67
5	60	59	63	60	58	62	60	58	58	56	58	56
6	71	74	69	68	73	64	72	70	72	78	70	69
7	65	66	64	62	62	68	70	65	63	64	65	63

whom readings were obtained for the previous month, and one the percentage in those from whom readings were obtained for the subsequent month. The mean of these two averages was taken. The hemoglobin curve obtained for the control group is shown in chart 2; although considerably higher, it corresponds closely to that shown by Mackay.

In this chart, the hemoglobin curve obtained for our control subjects is compared with those recorded by other recent investigators. When Mackay's [11] revised figures for the percentage of hemoglobin in her untreated, artificially fed infants are converted into grams, it may be noted that her values for all ages are from 1.5 to 2 Gm. lower than those represented by the curve for our control group. Mackay's low values may be explained by the inadequate diet which her infants received and by the poverty which prevailed in the slum districts of the East End of London from which her infants came. It may also be noted that the results obtained with our controls occupy an intermediate position among those recorded by the three American investigators and that the curve obtained

10. Rabinowitch, I. M.: Variations of the Percentage of Hemoglobin in Man During the Day, J. Lab. & Clin. Med. **9**:120 (Nov.) 1923. Dreyer, G.; Bazett, H. C., and Pierce, H. F.: Diurnal Variations in the Haemoglobin Content of the Blood, Lancet **2**:588 (Sept. 18) 1920.

11. Mackay, H. M. M.: The Normal Haemoglobin Level During the First Year of Life; Revised Figures, Arch. Dis. Childhood **8**:221 (June) 1933.

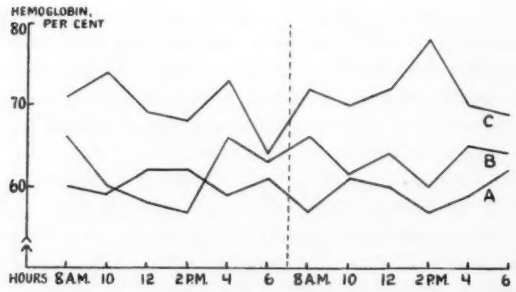

Chart 1.—Variations in the percentages of hemoglobin of 3 infants, as determined every two hours for two periods of twelve hours each. *A* represents the values for infant 1 (table 1); *B*, those for infant 3, and *C*, those for infant 6. In this chart and in the accompanying charts, a reading of 17.2 Gm. per hundred cubic centimeters of blood is represented by 100 per cent (Sahli scale).

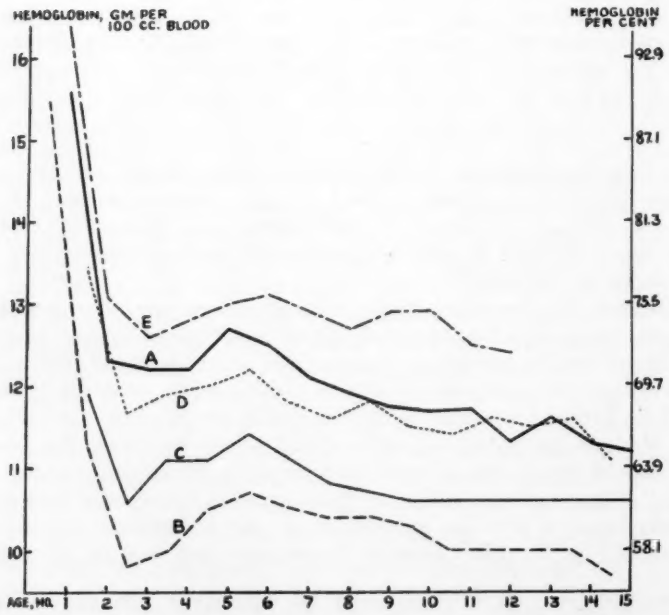

Chart 2.—Monthly variations in the average hemoglobin level, expressed in grams per hundred cubic centimeters of blood and in percentage, of our control group and of the control groups of other investigators. *A* represents the hemoglobin level of our group; *B*, that of Mackay's; *C*, that of Kato's; *D*, that of Elvehjem's, and *E*, that of Merritt's.

by Elvehjem [12] closely approximates our own. Merritt and Davidson,[13] at the Vanderbilt Clinic in New York, observed 73 normal infants from birth through the first year of life. These infants were chiefly from the poor or underprivileged classes. Kato [14] studied, from birth to the end of the second year, 780 infants attending the welfare clinics of the University of Chicago.

In only 2 instances did the hemoglobin value for the infants of our control group who were past the age of 5 months fall at any time to a level between 7 and 8.5 Gm.; in 13 cases, it fell, at some time during the period of observation, to a level between 8.5 and 10 Gm. In 11 cases the hemoglobin content at the age of 1 year was 12 Gm. or higher. It was found that if the hemoglobin value at the age of 1 month was high, it usually did not fall below 12 Gm. at the age of from 2 to 3 months and tended to remain even higher during the second half of the first year. Suppurative infections, such as otorrhea, boils and abscesses, had the greatest depressing effect on the percentage of hemoglobin. An infection of long duration, such as pertussis, lowered the amount of hemoglobin little, if at all. If the infection, particularly a suppurative one, occurred at a time when the hemoglobin is normally at a low point, as at the age of from 2 to 3 months or at that of about 1 year, the resulting anemia was greater than at other periods.

RESULTS

Effect of Iron on Hemoglobin.—The treatment of 69 patients with iron raised the percentage of hemoglobin in the blood after the age of from 3 to 4 months. In chart 3 is shown graphically the average percentage of hemoglobin at each of the first fifteen months of life for the controls as well as for the children treated with iron. Two curves are shown for the series receiving iron. The curve *A* indicates the average percentage of hemoglobin for the group given 1.5 grains of metallic iron daily, and *B*, that for the group given 3 grains. As may be noted in the chart, there was no sustained difference between the amounts of hemoglobin of the two groups receiving iron. However, a statistically significant difference is to be seen between the hemoglobin values for the controls and those for the groups receiving iron. It may be seen from chart 4 that the average hemoglobin value for the two groups receiving iron fell to 12.5 Gm. at the age of 2 and of 3 months, rose until it reached 13 Gm. at 4 months and then remained between 13.4 and 12.7 Gm. until the age of 15 months. Chart 4 also shows that the values for Mackay's group receiving iron, although considerably elevated above those for her control group, only approximated those obtained with our controls. This lower value was probably due to the smaller amount of iron given.

12. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D. R.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105 (July) 1933.

13. Merritt, H. K., and Davidson, L. T.: I. The Blood During the First Year of Life, Am. J. Dis. Child. **46**:990 (Nov.) 1933.

14. Kato, K., and Emery, O. J.: Haemoglobin Content of Blood in Infancy: Study of 780 Cases from Birth to Two Years, with 1065 Determinations, Folia haemat. **49**:106, 1933.

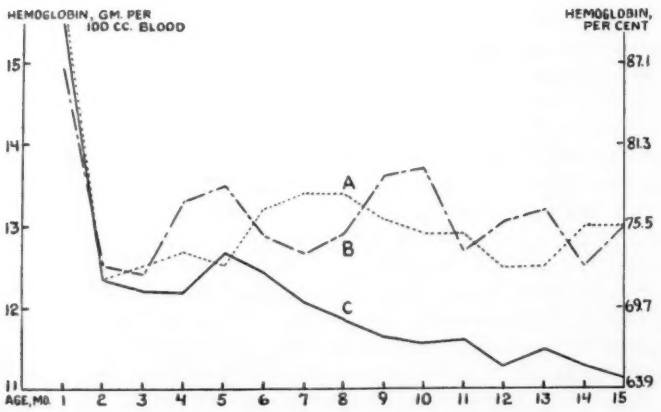

Chart 3.—Effect on the hemoglobin content, expressed in grams per hundred cubic centimeters of blood and in percentage, of the addition of iron to the diet. *A* represents the average hemoglobin content over a period of fifteen months of a group of infants receiving the equivalent of 1½ grains of metallic iron daily; *B*, that of infants receiving 3 grains of iron, and *C*, that of the control group.

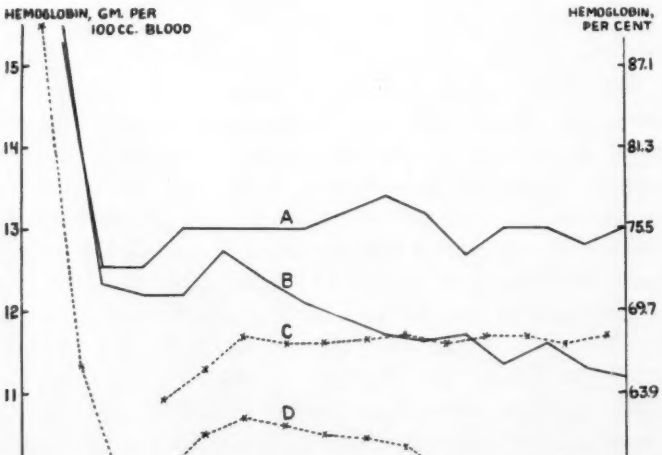

Chart 4.—Comparison of the average hemoglobin content, expressed in grams per hundred cubic centimeters and in percentage, of the infants in the control groups and those treated with iron in two series. *A* represents the average hemoglobin content of the entire group receiving iron in our series; *B*, that of our control group; *C*, that of Mackay's group receiving iron, and *D*, that of Mackay's control group.

Effect of Copper on Hemoglobin.—The addition of iron and copper to the diet of 95 children raised the amounts of hemoglobin to values slightly higher than those for the group receiving iron alone. In chart 5 it is to be noted that the average hemoglobin content of the group of infants receiving twice the dose of iron and copper reached a slightly higher level, especially at the age of from 9 to 12 months, than that of the group receiving half the dose. It is to be noted from chart 6 that the hemoglobin value for both the group receiving iron and that given copper dropped to about the same level at the age of from 2 to 3 months as did the value for the control group, even in those cases in which the medication had been instituted in large doses shortly after birth. Twenty-one infants, distributed evenly among the three groups,

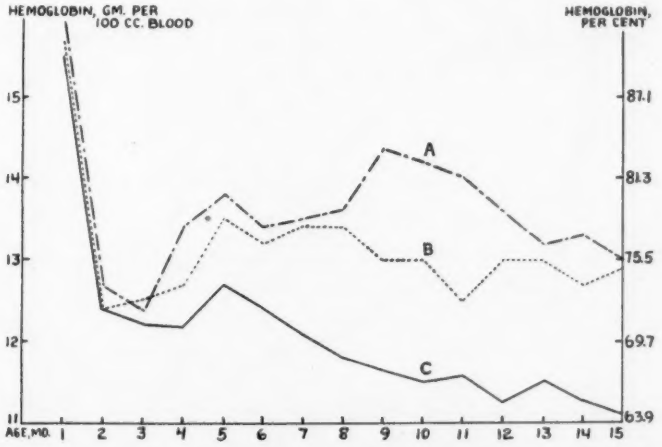

Chart 5.—Effect on the hemoglobin content, expressed in grams per hundred cubic centimeters of blood and in percentage, of the addition of twice the amounts of iron and copper to the diet. *A* represents the average hemoglobin content for a period of fifteen months of the group of infants receiving daily one-thirty-second grain of copper and 3 grains of iron; *B*, that of the group receiving one-sixty-fourth grain of copper and 1½ grains of iron, and *C*, that of the control group.

were observed after the age of 15 months, and the estimation of hemoglobin repeated from three to five months later. It was found that the average value for hemoglobin in the control group had advanced slightly from its low level of 11.2 Gm., but had not approximated that in the other two groups, which still averaged 12.5 Gm. In both the group given iron and that given copper and iron, the hemoglobin value for an individual infant was at no time much lower than 10.3 Gm. This high level was held through the course of the most severe infection. Frequently the hemoglobin reading remained high, in spite of the infection. Even in those cases in which the hemoglobin value was

greatly lowered, it usually rose after the infection subsided. In both of the treated groups, the maximum rise in the amount of hemoglobin occurred at the age of from 8 to 9 months, after which it fell slightly. There was a striking difference between the general appearance of the treated infants and that of the controls. The color of the former was much better, and the infants appeared brighter and more active, especially those given copper. The number of teeth which had erupted at the age of 1 year was the same for all the groups—four teeth as an average.

Effect of Iron and Copper on Weight.—The effect on weight of the addition of iron and copper to the diet was determined in the following manner: Each infant was weighed as nearly as possible on its monthly birthday. Curves were constructed showing the average weights of the

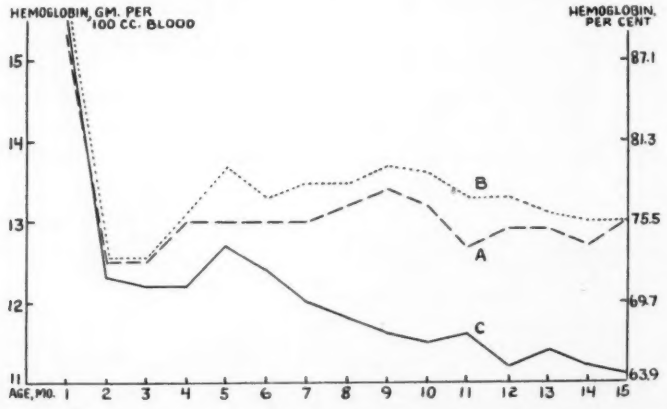

Chart 6.—Effect on the hemoglobin content, expressed in grams per hundred cubic centimeters of blood and in percentage, of the addition of iron and of copper and iron to the diet. *A* represents the hemoglobin content for a period of fifteen months of the group of infants receiving iron; *B*, that of the group receiving copper and iron, and *C*, that of the control group.

infants in the three groups (chart 7). From these it is seen that at the ages of from 8 to 10 months and from 12 to 14 months inclusive the children receiving iron weighed slightly less than the controls, and those receiving copper weighed from about 8 to 12 ounces (226 to 340 Gm.) more.

Morbidity Rate.—In table 2, the effect of the medication on the morbidity rate is recorded. The total number of available patients was 233; 69 of these were controls, 69 were in the group receiving iron and 95 in the group receiving iron and copper. No child was included in the control group who had been under observation for less than three months, or in the group receiving iron or iron and copper, respectively,

if it had received treatment for less than one month. We were fortunate in being able to observe closely the incidence and severity of the infections appearing among these children. Daily temperature charts were kept for each infant, nurses' notes recorded and, in addition to our own, rounds made several times a week by the visiting pediatrician. In the table of morbidity rates (table 2) a slight difference appears in the total number of infections of the respiratory tract occurring in the three groups. The incidence of infections of the respiratory tract is 9 per cent less in the group receiving iron than in the control group, and 13 per cent less in the group receiving copper.

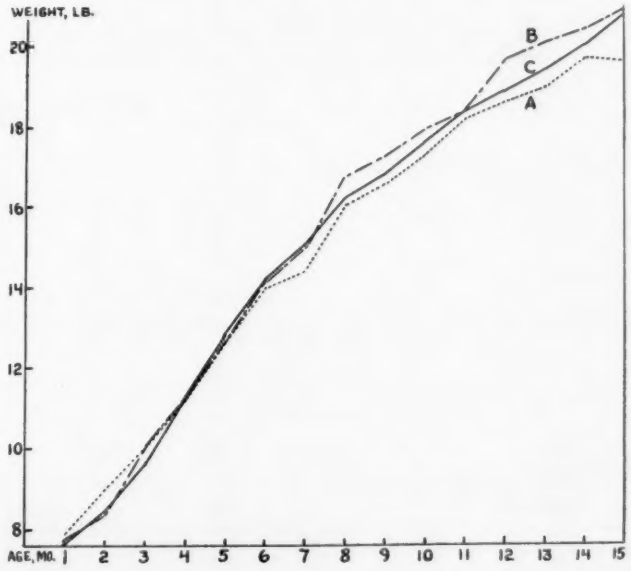

Chart 7.—Comparative average weights, expressed in pounds, for a period of fifteen months of the infants receiving iron (*A*); of those receiving copper and iron (*B*) and of the controls (*C*).

When the infections of the respiratory tract were classified, it was found that a greater number of attacks of nasopharyngitis occurred in both the group given iron and that given copper than in the control group. Fewer attacks of bronchitis and of otorrhea occurred in the group receiving iron and in that receiving copper than in the control group, and fewer cases of pneumonia were noted in the group given copper. That is, there was a considerable decrease in the frequency of the more severe infections of the respiratory tract among the infants of the treated groups, particularly in the group given copper. The incidence of these infections was 28 per cent less in the group given

iron, and 42 per cent less in that given copper, than in the control group. The frequency of diarrhea was the same in the three groups. Most of the cases of diarrhea were parenteral. No severe cases of summer diarrhea were encountered. The frequency of infectious fevers was 9 per cent less in the group given iron than in the control group, and 20 per cent less in the group given copper. The number of infections of the skin was 17 per cent greater in the group given iron than in the control group and 23 per cent less in the group given copper. The total number of infections occurring was 5 per cent less in the group given iron than in the control group, and 15 per cent less in the group given copper. In the groups receiving iron and iron and copper, respectively,

TABLE 2.—*Morbidity Rate* Due to Infections Occurring Among 233 Infants*

	Controls	Infants Treated with Iron	Infants Treated with Iron and Copper
Number of infants	69	69	95
Average period of observation per infant, months	8.6	9.4	9.1
Infection of respiratory tract			
Nasopharyngitis	11.1	13.7	14.7
Bronchitis	6	3.5	3
Pneumonia	2	2.4	1.3
Otorrhea	10.3	7.2	6.3
Infections of digestive tract			
Diarrhea	3.3	3.4	3.3
Incidence of specific infectious fevers			
Varicella	5.2	6.1	4.3
Measles	2	1.4	0.9
Pertussis	5	3.5	3.9
Scarlet fever	0	0	0.1
Nasal diphtheria	0.5	0.4	0.7
Erysipelas	0	0.1	0.2
Infections of the skin			
Boils and abscesses	4.7	5.5	3.6
Cervical adenitis	0	0.6	0.3
Total number of febrile attacks (tem. 100 F. or over)	170	169	155
Total number of infections	50.1	47.8	42.6

* Expressed as the number of attacks per month per hundred cases.

no suggestion of an initial superiority over the control group was found as regards weight or age. As a criterion of the severity of these illnesses, the duration of each of the various elevations of temperature was noted (table 3). The total elevation of temperature for the group receiving copper was 9 per cent less than that for the control group. As judged by the elevations of temperature, the greatest number of, and the most severe infections, occurred between the ages of 9 and 15 months.

MORTALITY RATE

In the computation of the number of deaths in each group as shown in table 4, none was included which occurred before the age of 3 months. Ten deaths (14.5 per cent) occurred among the 69 infants of the control group. The ages at death were as follows: Two patients were 3 months

old; 1, 7 months; 2, 8 months; 2, 10 months; 1, 11 months; 1, 13 months, and 1, 14 months. Five of this group died of bronchopneumonia which followed pertussis.

Eight deaths (11.6 per cent) occurred among the 69 infants of the group receiving iron. The ages at death were as follows: Three patients were 3 months old; 1, 5 months; 1, 9 months; 1, 13 months, and 2, 15 months. Five of this group died of bronchopneumonia following pertussis.

Six deaths (6.3 per cent) occurred among the 95 infants of the group receiving iron and copper. The ages at death were as follows:

TABLE 3.—*Number of Febrile Attacks* (Temperature of 100 F. or Over) Among 233 Infants*

Temperature, F.	Controls, per Cent	Infants Given Iron, per Cent	Infants Given Iron and Copper, per Cent
100	100	88	84
101	28	30	30
102	21	24	24
103	11	15	11
104	7	10	5
105	2	2	1
106	1	0	0
Total number of febrile attacks	170	169	155

* Expressed as the number of attacks per month per hundred cases.

TABLE 4.—*Mortality Among 233 Infants*

	Controls	Infants Receiving Iron	Infants Receiving Iron and Copper
Number of infants	69	69	95
Number of deaths among total number of infants	10	8	6
Mortality rate, per cent	14.5	11.6	6.3

Two patients were 3 months old; 1, 4 months; 1, 6 months; 1, 7 months, and 1, 10 months. Only 1 of these, an infant of 7 months, died of bronchopneumonia following pertussis; the other deaths resulted chiefly from repeated infections of the upper respiratory tract, complicated by otorrhea, boils and terminal pneumonia.

The mortality figures definitely indicate that the group receiving copper showed an increased resistance to severe infections. Not only was the mortality rate in this group decreased by one-half, as compared with that of the control group, but of 32 infants in whom pertussis developed, only 1 died after an attack. On the other hand, of the 29 infants with pertussis in the control group, and of the 23 in the group receiving iron, 5 in each group died.

Postmortem Analyses of Livers for the Presence of Iron and Copper.—Schwartz [15] studied histologically the livers and the spleens of several infants. He noted that the maximum amounts of iron were obtained from the livers of infants dying between the ages of 4 and 10 weeks. In infants past the age of 5 months, he observed a gradual decrease in the amount of iron, and in those 8 months old or younger, both organs were iron-free. Parsons [16] cited the work of Ramage and his co-workers, who made spectographic examinations of a large series of human livers. They found that copper and iron are the only metals stored as reserve materials in the liver during fetal life, and that the amounts of these reach their peak at birth. The iron and copper contents of the liver steadily diminish after birth and reach stable values between the ages of 12 and 18 months. The literature in general is not in agreement on the question of the storage of iron in early infancy.

It was considered of interest to study the effect of the administration of iron and copper on the storage of these elements in the liver. To this end, 36 analyses [17] were made of the copper and iron contents of the livers obtained at autopsy in our series. The ages of the children at death varied from 11 to 480 days. No chemical or histologic relationship has as yet been found between the age of the child and the amount of iron and copper per kilogram of liver, or between the age and the total amount of iron present in the liver. This was the case whether the infant received no treatment, treatment with iron alone or treatment with iron and copper. The data, therefore, do not tend to support the view that iron is stored in the liver prior to birth in order to compensate for the deficiency immediately following. Our observations, of course, are few, and this is to be considered in their interpretation. Further, no histologic evidence of injury to the liver cells could be seen in the case of infants who had received iron or iron and copper. We hope to resume, in the near future, our investigation of the storage of iron in early infancy.

COMMENT

When the average amount of hemoglobin in the blood of the infants in our control group is compared with the values obtained by Mackay, it is found that in our group, despite the frequency of the infections common to children in large institutions, the hemoglobin level was higher.

15. Schwartz, P.; Baer, R., and Weiser, J.: Histological Studies on the Iron Metabolism in Early Infancy, Ztschr. f. Kinderh. **37**:67, 1924.

16. Parsons, L. G.: Anaemia in Childhood, Arch. Dis. Childhood **8**:119 (April) 1933.

17. Dr. A. F. Fowler and Dr. I. M. Rabinowitch of the department of metabolism of the Montreal General Hospital made the iron and copper analyses, respectively; Dr. J. E. Pritchard of the department of pathology made the histologic examinations.

The reason for this difference probably lies in the adequate diet which our infants received, in contrast to that of Mackay's infants, which consisted of milk alone prior to the age of 9 months. Her infants suffered not merely from physiologic anemia, which has been shown by various investigators to be common to all infants, but from a definite early nutritional anemia This fact may partially explain the more striking results which she obtained with the addition of iron. Again, it is striking that the hemoglobin curves for our institutionalized infants compare favorably with those obtained by other investigators. In a study of the individual cases in our control group, it is of interest that, despite the severest infections, the level of hemoglobin rarely fell below 8.5 Gm. and never below 7 Gm. These amounts contrast sharply with the levels in cases of nutritional anemia, in which the hemoglobin is frequently less than 7 Gm., particularly if the anemia is aggravated by an infection.

What is the significance of this anemia which is found during the latter half of the first year and throughout the second year of life? It is a normal phenomenon, as has been pointed out by a number of investigators and appears to a greater or lesser degree in all normal infants. The early addition to the diet of vegetables, fruits and cereals does not prevent it, nor is there evidence in the literature that this form of anemia is due to rickets or to the lack of any of the known vitamins.

The steady decrease in the amount of hemoglobin from birth to the age of 3 months is probably due to two factors: The first is the destruction of blood cells, which in the normal infant begins shortly after birth, and which is due to the difference in the oxygen tension of the blood before and after birth (Goldbloom and Gottlieb [18]). This destruction ceases after a few weeks, and the iron resulting from the products of the destruction of the red blood cells is utilized by the active bone marrow in the formation of new blood cells. The second factor is the rapid increase in weight which occurs during the first four months, during which period the infant nearly doubles its weight at birth. At the same time, the volume of blood is doubled, and although the total amount of hemoglobin may remain unchanged or be somewhat increased, the percentage is greatly reduced. Even the addition to the diet of large doses of iron and copper almost from birth does not alter the essential characteristic variations in the hemoglobin curve during the first year of life, although they take place at a higher level. Does this increase in the value for hemoglobin offer an advantage to the child? Mackay was emphatic in her conclusions that it is of distinct value in increasing the general resistance to infections. She pointed to a decrease of 50 per cent in the morbidity rate in the group of treated infants. Our figures,

18. Goldbloom, A., and Gottlieb, R.: Icterus Neonatorum, Am. J. Dis. Child. **38**:57 (July) 1929.

although much less striking, point to a similar conclusion especially for the group receiving iron and copper. More striking in our series was the decrease by one-half of the total mortality rate in the group receiving iron and copper. This advantage was particularly evident in the mortality rate from whooping cough. The reason for this is not clear at present and requires further investigation. Merritt,[19] however, in a comparative study of treated and untreated premature and immature infants, found that the infants treated with iron, although having a considerably increased percentage of hemoglobin, showed a higher incidence of infection and no greater increase in weight than did the control infants. There were only 2 deaths in her total series of 99 cases.

It must be emphasized that the children in Mackay's study were drawn from among the poor of the East End of London and were, to begin with, nutritionally below par. Those of our series, although receiving an adequate diet and living under the most hygienic conditions, showed the mental and physical retardation common to all children in large institutions for foundlings, in which the stimulating personal attention and devotion of parents are unavoidably lacking.

SUMMARY AND CONCLUSIONS

A series of observations on infants receiving either iron or iron and copper is reported, and the data are compared with those for a control group receiving no medication. The observations included those on (1) the hemoglobin value, (2) the weight, (3) the morbidity rate, (4) the mortality rate and (5) the postmortem chemical and histologic analyses of the liver for the presence of iron and copper. The assembled data are treated statistically and compared with the results obtained by other investigators in the field. The results of this study were as follows:

1. In a study of a series of normal children confined to an institution, the hemoglobin value was found to fall sharply from the high level at birth to approximately 12.2 Gm. at the age of from 2 to 3 months; it rose slightly at the age of 5 months, and then fell slowly to an average level of 11.2 Gm. at the age of 1 year.

2. A group of children receiving daily from 1½ to 3 grains of iron in the form of ferric glycerophosphate showed at the age of 1 year an average hemoglobin value 15 per cent higher than that of the controls.

3. A group of children receiving daily from 1½ to 3 grains of iron supplemented with from $\frac{1}{60}$ to $\frac{1}{32}$ of a grain of copper sulphate, showed an average hemoglobin value 19 per cent higher than that of the control group.

19. Merritt, K. K., and Davidson, L. T.: Blood During the First Year of Life: II. The Anemia of Prematurity, Am. J. Dis. Child. **47**:261 (Feb.) 1934.

4. At the ages of from 8 to 10 and from 12 to 14 months, the average weight of the group receiving iron was slightly less than that of the control group, and that of the group receiving copper was from 8 to 12 ounces more.

5. As regards the incidence and severity of infections, the children treated with iron showed only a slight advantage over the untreated controls, while those treated with iron and copper showed a more definite advantage.

6. As shown in a study of the mortality rate, the children treated with iron showed a moderate advantage over the untreated controls, and those treated with iron and copper a striking advantage. This advantage for the group receiving copper was especially evident in the mortality rate from pertussis. No explanation of this effect of copper is at present offered.

7. In the cases of infants who died, no relationship could be demonstrated between the ages and the amount of iron and copper per kilogram of liver, or between the age and the total amount of iron present in the liver. This was true regardless of whether no treatment had been received, or whether the treatment had been with iron alone or with iron and copper.

Professor Howat, assistant professor of mathematics, McGill University, criticized the statistical use of the data and the preparation of the curves; the Grey Nuns, the nurses at the Crèche Youville and Dr. Daniel Longpré, the attending pediatrician, greatly facilitated the work.

INFLUENCE OF ACUTE INFECTION AND ARTIFICIAL FEVER ON THE PLASMA LIPIDS

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The chance observation of a precipitous drop in the plasma lecithin values of several epileptic patients in whom there developed acute infections during studies on the blood lipids suggested the investigation of the various lipid fractions of the blood plasma in acute infections and in artificially induced fever. In a previous study [1] we presented the results in a preliminary series of cases of various acute infections. Not only the plasma lecithin but the plasma cholesterol and fatty acids were determined. In every case, at the height of the disease there was a definite lowering of the plasma lecithin and cholesterol. The values became subnormal, but they arose again during convalescence, approaching or reaching normal. Changes in the total fatty acid values paralleled those for the lecithin and the cholesterol in most instances.

Although the literature revealed that the plasma cholesterol values had previously been found to be lowered in certain acute infections,[2] a thorough investigation of all the plasma lipids had never been undertaken. A more elaborately controlled study was therefore made to determine the degree of correlation between changes in the various plasma lipids and such factors as diet, body temperature, severity of clinical signs and alterations in the leukocyte response. It was hoped that the study might also further the knowledge concerning the chemical changes associated with the immune processes occurring in acute infections.

From the Department of Pediatrics, the University of Minnesota.

Presented at the Fifth Annual Meeting of the Society for Pediatric Research, New York, May 6, 1933.

1. McQuarrie, Irvine, and Stoesser, A. V.: Influence of Acute Infection and of Artificial Fever on Plasma Lipoids, Proc. Soc. Exper. Biol. & Med. **29**:1281, 1932.

2. Denis, W.: Cholesterol in Human Blood Under Pathological Conditions, J. Biol. Chem. **29**:93, 1917. Stepp, W.: Ueber den Cholesteringehalt des Blutserums bei Krankheiten, München. med. Wchnschr. **65**:781, 1918. Kipp, H. A.: Variation in the Cholesterol Content of the Serum in Pneumonia, J. Biol. Chem. **44**:215, 1920. Achard, C.; Grigaut, A.; Leblanc, A., and David, Marcel: L'équilibre lipoidique du sérum sanguin dans les maladies aigües, J. de physiol. et de path. gén. **26**:415, 1928.

MATERIALS AND METHODS

The lipid fractions of the plasma were determined on a series of thirty-six hospital patients. The subjects were all children, ranging in age from 15 months to 14 years. To rule out the possible influence of a variation in diet, fourteen patients with acute infections were studied. There were four patients with nasopharyngitis and tonsillitis, one with otitis media, one with cervical adenitis, two with uncomplicated lobar pneumonia, three with lobar pneumonia complicated by otitis media, peritonitis or empyema and three with bronchopneumonia. The patients were placed on a special maintenance diet containing adequate amounts of water and vitamins and 2 Gm. each of protein and fat and 5 Gm. of carbohydrate per kilogram of body weight. The diet was started as soon as possible after the patient was admitted to the hospital. The same amount and quality of food were given at each meal. The meals were equally spaced at four hour intervals, and between times the subject was permitted to take a moderate amount of water. During the period of observation no medication was given. The administration of fluid or blood subcutaneously, intramuscularly or intravenously was not permitted. The first sample of blood was obtained at the height of the disease after the subject was having no difficulty in taking the proper amount of food. This usually occurred on or about the seventh day of the illness and from the second to the sixth day after the diet had been started. The second sample of blood was drawn on about the ninth day of convalescence.

The time at which the sample of blood was collected was recorded, together with the rectal temperature and the white blood corpuscle count. In many instances determinations of the hemoglobin content were also made, in order to check the factor of blood concentration. As far as possible the samples of blood were obtained under identical conditions as regards the time of day and the relationship to meals.

The blood was collected in specially cleaned tubes, and as soon as possible the plasma was separated from the cells by centrifugation. The plasma was quickly poured into the alcohol-ether mixture, and the various chemical analyses were made according to the methods of Bloor.[3] In spite of the precautions taken in drawing the blood, occasionally plasma samples were tinged pink, indicating hemolysis of some of the cells. They were all discarded and fresh blood was obtained.

Thirteen patients with acute infections, including three with nasopharyngitis, one with otitis media, one with cervical adenitis, three with uncomplicated lobar pneumonia, three with lobar pneumonia complicated by otitis media and two with bronchopneumonia, did not receive the special diet. They were given the ordinary mixed diets of the hospital. During the height of the infection they received a bland diet divided into three meals equally spaced, while during convalescence the full diet of the hospital was taken without difficulty. In this group more food was eaten during convalescence than during the period of acute illness. The first sample of blood was usually obtained about the fifth day of the disease and the second sample about the eighth day of convalescence. The time of day for the withdrawal of the blood was the same in each instance, so that the relationship to meals was not altered.

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3. Bloor, W. R.: The Determinations of Cholesterol in Blood, J. Biol. Chem. **24**:227, 1916; The Determination of Small Amounts of Lipid in Blood Plasma, ibid. **77**:53, 1928; The Oxidative Determination of Phospholipid (Lecithin and Cephalin) in Blood and Tissues, ibid. **82**:273, 1929.

To ascertain the influence of fever alone as against that of the other effects of infection, nine subjects with chronic afebrile disorders in whom fever was induced by various methods were studied. Six were given the special diet previously described, and three received the ordinary hospital diet. Samples of blood were obtained before, during and after the febrile periods. The duration of the more or less sustained artificially induced fever ranged from one to seven days. There were one case of chronic arthritis with diathermy fever, three cases of chorea with fever produced by injection of phenyl-ethyl-hydantoin, two cases of chorea with foreign protein fever induced by the injection of triple typhoid vaccine and three cases of congenital syphilis with malaria. The patients in the last group were inoculated with Plasmodium malariae as a therapeutic measure.

RESULTS

For the sake of clearness the results representing all the determinations made on the thirty-six children have been condensed on eight charts which are largely self-explanatory.

In charts 1 and 2 are the data from the studies made on the fourteen patients receiving the special diet. The six subjects with infections of the upper respiratory tract were placed in one group and the eight with pneumonia in another. Charts 3 and 4 present data from the studies on the thirteen patients not receiving the special diet, of whom five had infections of the upper respiratory tract and eight had pneumonia. With one exception, the values for cholesterol, lecithin and total fatty acid were all lower during the height of the disease than during convalescence. In some instances the values were low in the febrile period of the illness; in other cases they were not depressed very far below the lower limit of normal. Some of the lowest values rose rather steeply in the convalescent period to attain a level within the range of normal. In a number of cases, however, the samples of blood were secured before the plasma lipids had had sufficient time to reach the normal levels. All the values which were not very low at the height of the infection returned rather quickly to a normal level in convalescence.

A comparison of the subnormal values observed during the febrile period of the disease for the children with infections of the upper respiratory tract receiving the special diet with those for the children not receiving the special diet showed no significant difference. The same conclusion could be drawn from a comparison of the groups with pneumonia. During the convalescent period the rise in the lipid fractions was approximately the same for the corresponding groups. This was especially true of the cholesterol and the lecithin fractions, although the total fatty acids of the plasma showed a similar trend. From these observations, it is apparent that diet had no marked influence on the results.

High temperatures occurring in patients who were very ill were not necessarily accompanied by low values for the various lipid fractions,

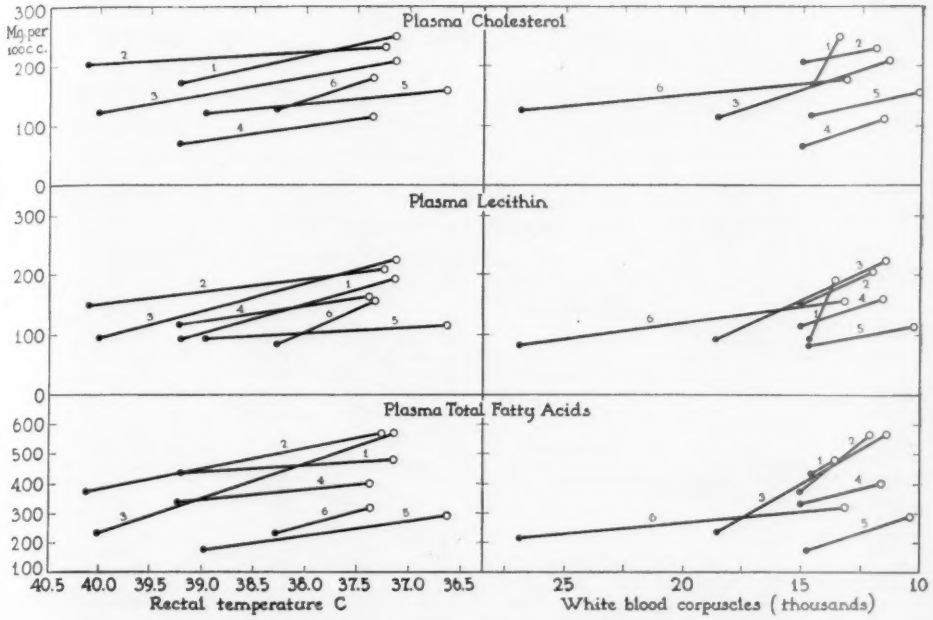

Chart 1.—The plasma lipid values in relation to the rectal temperature and the white blood corpuscle count in six patients with infections of the upper respiratory tract. The subjects received the special maintenance diet. The solid dots represent the height of the disease and the open circles the period of convalescence.

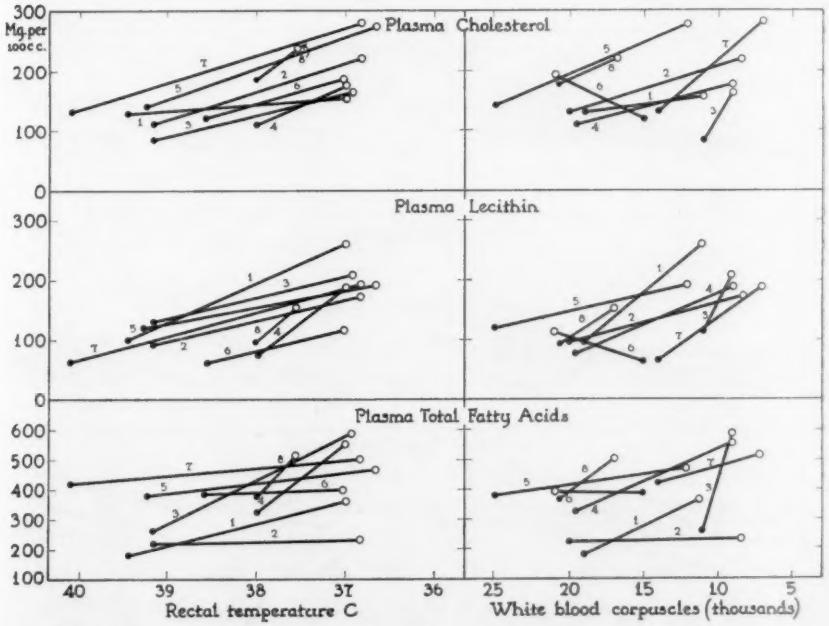

Chart 2.—The various plasma lipid fractions in eight patients with pneumonia, who received the special maintenance diet. The solid dots represent the height of the disease and the open circles the period of convalescence.

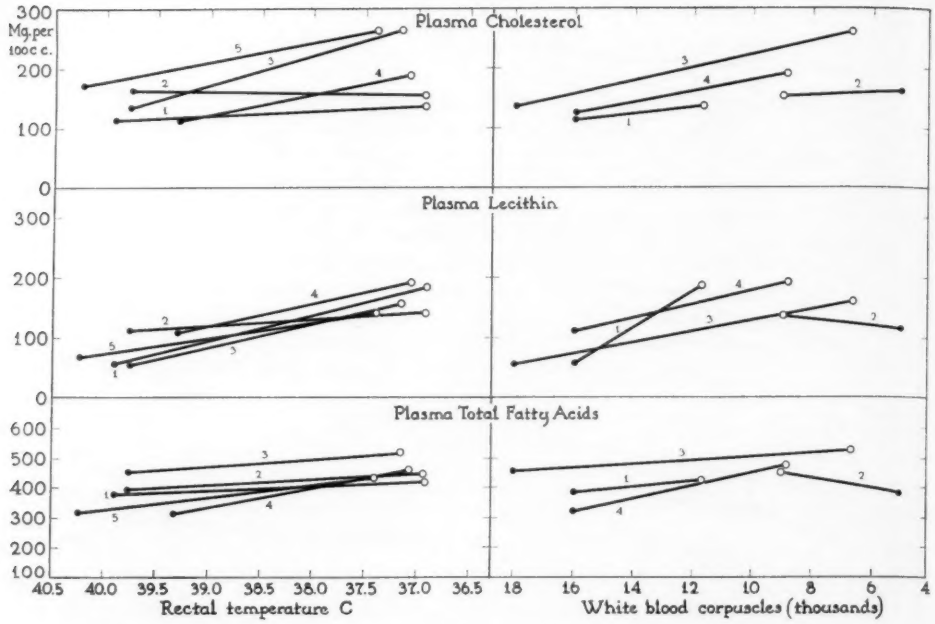

Chart 3.—The plasma lipid values in relation to the rectal temperature and the white blood corpuscle count in five patients with infections of the upper respiratory tract. The subjects received the ordinary mixed diets of the hospital. The solid dots represent the height of the disease and the open circles the period of convalescence.

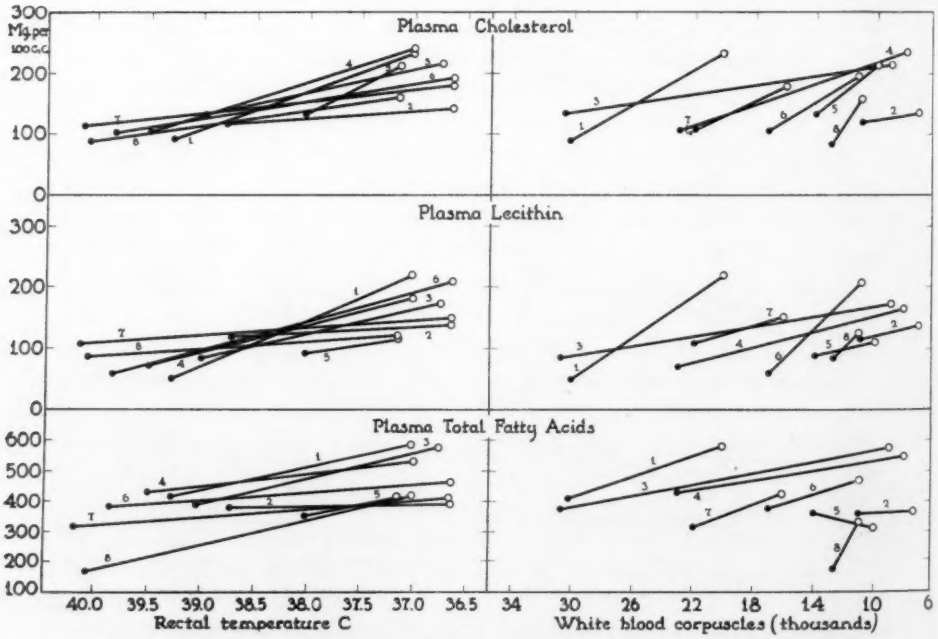

Chart 4.—The various plasma lipid fractions in eight patients with pneumonia who received the ordinary mixed diets. The solid dots represent the height of the disease and the open circles the period of convalescence.

and slightly elevated temperatures at the height of some of the milder infections were not an indication of small changes in the lipid content of the blood plasma. In some instances the reverse was true, as, for example, in case 3, chart 1. Here the temperature rose as high as 40.2 C. (104.4 F.), but the cholesterol level dropped very little, to 203 mg. per hundred cubic centimeters of plasma. In case 4, chart 2, in spite of the fact that the temperature was only 38.1 C., the cholesterol content of

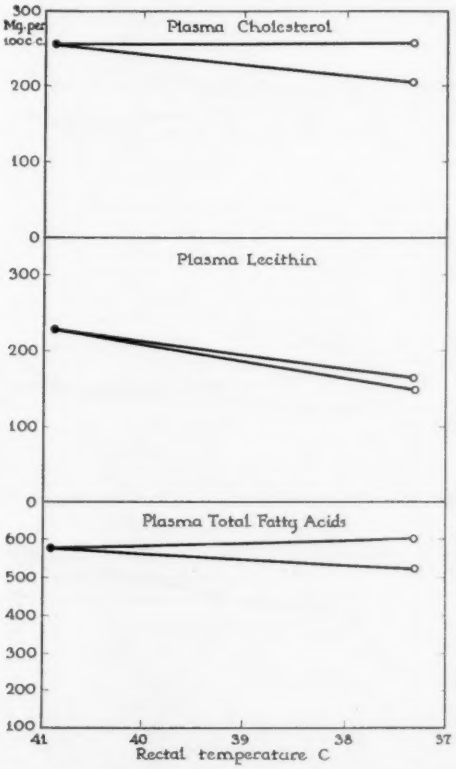

Chart 5.—The effect of diathermy fever on the plasma lipids in a case of chronic arthritis. The solid dot represents the period of fever and the open circles the afebrile period.

the plasma fell to a low level, 114 mg. In a few cases the lecithin values showed to a less extent the same variation to temperature. There was no constant relationship between the height of the fever or the severity of the clinical signs and the degree of hypocholesteremia or hypolecithinemia in the cases studied. The same was true for the low total fatty acid values.

The total white blood corpuscle count varied inversely with the lipid content of the blood plasma. The very high counts occurring at the

height of the infection were, however, not all associated with the lowest lipid figures obtained. In some instances leukocyte counts which were only slightly increased during the febrile period were accompanied by rather low lipid values. The rapid fall of the high white blood cell count to within the normal range in the convalescent period was usually, however, an indication that the lipid content of the blood plasma had undergone a marked change and that it had now risen to a level close

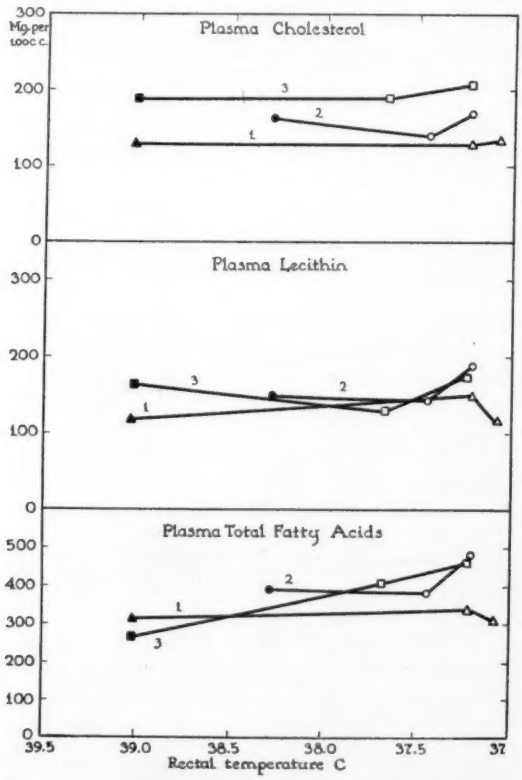

Chart 6.—Effect of phenyl-ethyl-hydantoin fever on the plasma lipid values in three patients with chorea. The solid figures represent the period of fever and the open figures the febrile processes.

to or within the limits of normal. In some cases, however, a very small elevation in the white blood cell count existed at the height of the disease, and only a slight drop occurred during convalescence, but this was associated with a marked change in the lipid values.

There were two cases in which the leukocyte counts were higher in the convalescent period than at the height of the illness. The behavior of the plasma lipids in these subjects was interesting.

The first patient (case 6, chart 2) showed the usual lowering of the cholesterol and lecithin values during the febrile period. The return to normal was, however, quite slow. The subject was a girl, 3 years old. She was admitted to the hospital with a diagnosis of bronchopneumonia. At the time the first sample of blood was obtained, she was not very ill. The temperature was only slightly elevated, to 38.4 C. (101.1 F.), and the white blood cell count was 15,000. After the temperature had been normal for nine days, the second sample of blood was secured. At that time the leukocyte count averaged 21,800. A thorough clinical study revealed

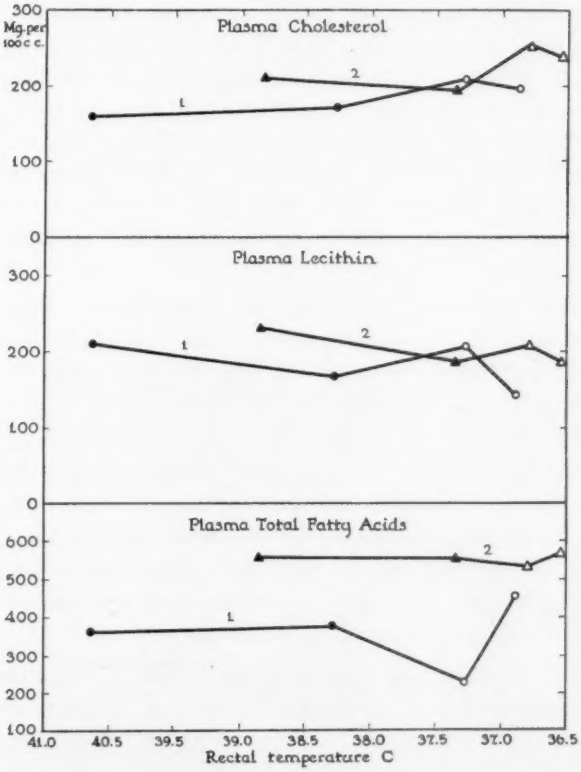

Chart 7.—The effect of foreign protein fever on the plasma lipids in two patients with chorea who received inoculations of triple typhoid vaccine. The solid figures represent the period of fever and the open figures the afebrile period.

no definite cause for the rise in the white blood corpuscle count, although a small patch of unresolved pneumonia was suspected.

In the second patient (case 2, chart 3) the cholesterol content of the plasma was highest in the febrile period. This was the one exception to the observation that the lipid fractions were all lower during the height of the infection than during convalescence. The lecithin and total fatty acid values did not, however, parallel that of the cholesterol. The subject was a girl, 5 years old, who was admitted to the hospital with a diagnosis of influenza. The temperature was 39.8 C.

(103.6 F.), and the leukocyte count was 4,300. In a few days, in spite of the apparent leukopenia, the diagnosis was changed to acute nasopharyngitis and tonsillitis. Twelve days after the temperature had returned to and remained normal, the white blood corpuscle count had increased to 8,800. At that time a roentgen study of the sinuses showed definite evidence of infection in the maxillary antrums.

In connection with the first case the observation was made that although the plasma lipid values were low during the febrile period they did not increase rapidly enough in the convalescent period to reach the normal range before the second sample of blood was drawn. The same was true in four other subjects (case 5, chart 1, and cases 2, 7, and 8, chart 4). The lecithin values responded the least, and in these patients, in spite of the fact that the temperature had been normal for seven days, an infection was found to be present. In one instance there was an acute inflammation of the middle ear in which perforation of the tympanic membrane had not taken place, and in the remaining three an acute suppuration of the middle ear existed, with perforation of the tympanic drum.

The results presented in charts 5 to 8 indicate the determinations which were made on samples of blood drawn before, during and after artificially induced hyperthermia in the nine children with afebrile chronic disorders. In the first case (chart 5) the fever, which was of one day's duration, was produced by diathermy. The highest values shown in chart 5 under the heading "afebrile period" represent the blood plasma content of the various lipid fractions before the fever was induced. There was no significant lowering of the plasma lipid values during the height of the febrile period. In fact, the lecithin content of the plasma was lowest before and after the fever, which does not parallel the results obtained in the subjects with acute infections.

The three patients with chorea minor (chart 6) receiving phenyl-ethyl-hydantoin (nirvanol) responded to the drug with a febrile reaction lasting from two to three days. The results of the determinations on the samples of blood secured before, during and after the fever showed no change which would indicate that the hyperthermia made any great difference in the values. The lipid values remained more or less at a constant level. There was, however, one exception. This occurred in case 3, in which the total fatty acid value was lower during the febrile period than at any other time.

Two additional patients with chorea minor (chart 7) were inoculated therapeutically with triple typhoid vaccine, with a resulting foreign protein reaction. Samples of blood were taken on the fourth and on the seventh day of a period throughout which the temperature was elevated most of the time as the result of repeated inoculations. An analysis of the samples gave lipid values which differed in no significant

way from those secured before and after the foreign protein therapy. This is clearly illustrated in chart 7, in which are presented, first, the two values obtained for each lipid fraction of the plasma during the time when there was a more or less sustained foreign protein fever, and then the values in the periods before and after hyperthermia.

The three patients with congenital syphilis (chart 8) who were inoculated with P. malariae as a therapeutic measure were carefully

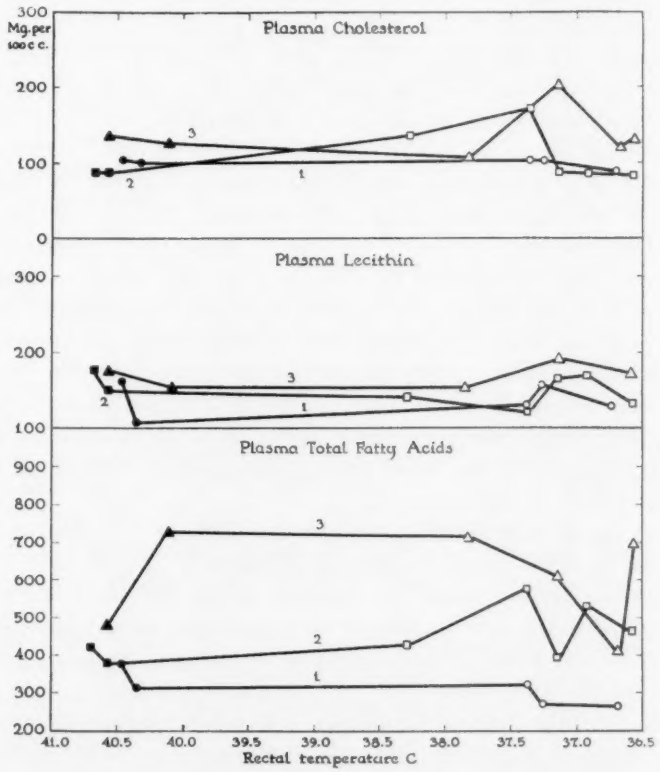

Chart 8.—The plasma lipid values in three patients with congenital syphilis inoculated with P. malariae. The solid figures represent the paroxysmal period and the open figures the afebrile period.

studied during the course of the treatment. Determinations were made at the height of two paroxysms of fever in each subject. In addition, samples of blood were secured from two patients before the paroxysms started, from all the patients during the afebrile intervals between paroxysms and from one patient after the disappearance of the malaria under quinine therapy. The results of the analyses of all the latter samples appear on chart 8 under the caption "afebrile period." A comparison

of all the lipid values of the paroxysmal period with those of the afebrile period reveals no outstanding difference, in spite of the fact that there was a tendency to hypocholesteremia in all the subjects during the malarial infection.

COMMENT

From the foregoing results it is evident that the various lipid fractions of the blood plasma tend to drop to subnormal levels during acute infections and that with recovery the values return to the normal range. On the assumption that diet might play an important rôle in producing these results, the samples of blood were collected in each instance at the same time in relation to the meals, which were served to the patients at definite intervals with no variation throughout the period of observation. In addition, about one half of the subjects received a special diet, which not only included the equal and constant spacing of meals but guaranteed the same daily intake of foodstuffs during the period of acute illness as well as during recovery. With these precautions the influence of diet emphasized by some writers was, to our satisfaction, ruled out. The diet did not alter in any significant way the large changes observed in our cases. Determinations of the hemoglobin content were made on the majority of the patients at the same time that the blood plasma was obtained. There was not much variation in a given case. In fact, the relative constancy of the hemoglobin values indicated beyond doubt that changes in the blood concentration played little or no part in the plasma lipid variations.

Fever per se was certainly not the cause of the low lipid values at the height of the disease, because the subjects with artificially induced hyperthermia did not show the constant fall in the lipid fractions so characteristic in the patients with acute infections. Even when the fever was more or less sustained for as long as seven days, no definite changes occurred in the lipid values.

With so little definite knowledge concerning the function of the lipids, especially of cholesterol and lecithin, it is rather difficult to evaluate our results in connection with the phenomena which go on in the body during an acute infection. The blood may simply act as a conveyer of the lipids as it does for other substances. Therefore, there may be a lack of supply at one end of the system, such as might occur with decreased absorption from the intestines, or there may be a greater demand at the other end in the tissues altered by the toxins of the acute infections. In the former case the blood would receive little lipid material, while in the latter instance there would be a decrease in the amount of blood fat. It has been stated, however, that any interference with proper lipid absorption from the intestines results in most cases in an increase in the value for blood fat. The liver has been mentioned as an organ which possibly influences the blood lipids once it is affected

by the bacterial toxins. Toxic changes in the liver are usually shown by an increase in the fat in the organ, and this condition tends to be associated with hyperlipemia rather than with a low lipid content in the blood plasma.[4]

It has been contended that lecithin takes part in the phenomena of immune reactions. This contention, first set forth by Bang,[5] has not received much support. Recent investigations in animals have shown that lecithin has no constant effect on bacterial toxins, and that it does not stimulate the formation of antibodies.[6] In some instances there appears to be a depressive action. Cholesterol, however, has been found to combine readily with bacterial toxins, thereby rendering them less toxic. Diphtheria toxin is partly neutralized by a weak colloidal suspension of cholesterol.[7] Cholesterol has been used to protect animals not only against the action of diphtheria toxin but against that of tetanus and of botulinus toxins.[8] The ingestion of the lipids, especially cholesterol, stimulates the formation of immune bodies and increases the ability of the animal to overcome an infection.[9]

As a whole the experiments on animals have revealed that the lipids may play a rather important part in the defensive mechanism of the organism.[10] In view of this observation, what is the significance of the low values found in man during an acute illness? This question cannot be answered from the data presented. However, some relationship can be considered to exist between the phenomena of immunity during an infection and the low lipid values. Lecithin, with its unfavorable influence on the formation of antibodies, has a low fraction as long as an infection is present. In some of our subjects, even though the temperature had returned to normal and the white blood cell count

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4. Peters, John P., and Van Slyke, Donald D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

5. Bang, Ivar: Die biologische Bedeutung der Lipoidstoffe, Ergebn. d. inn. Med. u. Kinderh. **3**:447, 1909.

6. (*a*) Suranyi, L., and Jarno, L.: Ueber den Einfluss der Lipoide auf die Toxinwirkung, Ztschr. f. Immunitätsforsch. u. exper. Therap. **57**:199, 1928. (*b*) Suranyi, L.: Immunkörperbildung lipoigefütterter Tiere, Ztschr. f. Immunitätsforsch. u. exper. Therap. **57**:185, 1928.

7. Tunnicliff, R.: Influence of Cholesterol on Phagocytosis, J. Infect. Dis. **33**:285, 1923.

8. Leupold, Ernst, and Bogendorfer, L.: Cholesterin Protects Against Infections, Deutsches Arch. f. klin. Med. **140**:28, 1922. Suranyi and Jarno.[6a]

9. Borchardt, W.: Beitrag zur Bedeutung des Cholesterins bei experimenteller Staphylokokkeninfektion der Katze, Klin. Wchnschr. **8**:1179, 1929. Reiter, Hans: Lipoidnahrung und Infektion, Klin. Wchnschr. **7**:589, 1928. Suranyi.[6b]

10. Brazil, V., and Vollard, J.: Ueber die Rolle der Lipoide in der Immunisierung bindende und entgiftende Eigenschaften der Lipoide: Lipoidimpstoffe, Ztschr. f. Immunitätsforsch. u. exper. Therap. **56**:191, 1928.

had fallen close to or within the normal range, the lecithin values did not rise rapidly. In all these patients, an infection still existed.

Cholesterol, on the other hand, has a great tendency to combine with bacterial toxins. The low values at the height of an acute infection in man may indicate that to a certain extent this combination is actually taking place, the cholesterol being utilized during the process of neutralization of the toxins produced by the invading organisms. The union could be either a phenomenon of absorption or a chemical reaction. It is difficult to say at this time just what the mechanism is. At any rate there appears to be considerable promise in this approach to the subject of the chemistry of immunity.

A still more thorough study of the plasma lipids might be of great value in revealing, at least in part, the mechanism of resistance of the host to an acute infection. One should not only investigate the changes in the total cholesterol values but those in the values for free cholesterol and the cholesterol esters. In addition, an examination of the variations in the degree of unsaturation of the fatty acids of the blood fat and of the plasma phospholipids should be made. This extensive study has been undertaken.

SUMMARY AND CONCLUSIONS

Following a preliminary investigation, a thorough study was made of the values for plasma lecithin, cholesterol and total fatty acids in each of thirty-six children, in order to determine the degree of correlation between changes in the various plasma lipids and such factors as diet, body temperature, severity of clinical signs and alterations in the white blood cell count.

Twenty-seven children had acute febrile infections. Fourteen of the subjects received a special, carefully regulated diet, while thirteen did not. Determinations were made during the period of acute illness and during the convalescent period. There was a definite lowering of the values for the plasma lipids at the height of the disease as compared with the levels obtained during convalescence. Diet had no demonstrable influence on the results.

The lowest lipid values were not always found in the subjects with the highest body temperatures or in those most acutely ill. There appears to be no constant relationship between the degree of hypolecithinemia and hypocholesteremia and the height of the fever or the severity of the clinical signs.

White blood cell counts were obtained in each instance at the time a sample of blood was collected for an analysis of the lipids. With but two exceptions the count varied inversely with changes in the lipid values. The highest leukocyte counts were, however, not necessarily found in the patients with the lowest lipid values.

There was a tendency for the lipid content of the blood plasma to rise very slowly and to remain below the normal range during the convalescent period if an infection still existed. This was especially true of the lecithin fraction.

Nine children had chronic afebrile disorders, and fever was induced by various methods in these subjects. Determinations which were made before, during and after the artificial production of high body temperatures revealed no significant lowering of the plasma lipids. Fever per se was therefore not responsible for the lowering of the various lipid constituents of the blood plasma of the subjects with acute infections.

The results presented in this communication are worthy of record, but their significance cannot be determined until further data have been obtained. Experiments on animals have already shown that the lipids are involved in some way in the phenomena of immunity, and in view of that fact our results may open another possible approach to a more complete investigation into the chemistry of immunity.

Further valuable data may be furnished by a more thorough study of the plasma lipids, which is now being undertaken. This study includes an analysis of the changes in the total cholesterol, the free cholesterol and the cholesterol esters and the variations in the degree of unsaturation of the fatty acids of the blood fat and the plasma phospholipids occurring during acute infections.

BASAL METABOLISM IN CHILDREN OF NORMAL AND OF SUBNORMAL INTELLIGENCE

WITH BLOOD CHOLESTEROL AND CREATININE VALUES

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WITH THE ASSISTANCE OF ARTHUR B. HAW, M.S., LANSING, MICH.

This study was stimulated by the lack of available data regarding the basal metabolism of children and its relationship to their mental status.

The work was conducted at the Michigan State School for Children, Coldwater, Mich., where I was resident physician during this investigation. The children were acclimated to the surroundings and had no fear of the hospital [1] where the metabolism tests were done, having been there on many previous occasions for the treatment of minor ailments and as patients. There was always a close contact between the child and the hospital staff. A friendly relationship prevailed at all times. The nature and purpose of the metabolism tests were explained to the children and soon they were cooperative and anxious to have the tests. Under such ideal conditions it was not difficult to obtain reliable data.

METHODS AND MATERIAL

The subject slept in the hospital over night, and the tests were run early in the morning, with the child in the postabsorptive state and in complete mental and physical relaxation. If the oral temperature was higher than 99 F., the test was postponed. Two determinations were made on the same morning on each child, each test lasting for six minutes, with a few minutes' interval between the two. The lowest reading was taken as the basal rate [2] for that morning. The tests were repeated on subsequent days as often as was deemed necessary, or until it was felt that the best conditions were met. The aim was to have the subject completely at ease, breathing quietly and regularly and showing no apprehension

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From the Michigan State Public School, Coldwater, Mich., and the Department of Pediatrics, University Hospital, Ann Arbor, Mich.

1. This was a forty bed hospital located on the grounds and served as the medical center for the institution.

2. The basal rate in the preliminary reading was often not the "true" basal rate, but was entered in the tables for a comparison of the data. Before a result was accepted as a "true" basal rate, it was essential that the child conform to the requirements outlined, with the oxygen consumption lines of the two readings of the same morning not showing a difference greater than 6 mm. On occasions the variations were greater. In such instances, if the child otherwise maintained basal conditions, the readings were accepted.

or fear during the test, with the pulse and blood pressure within normal limits. When these conditions were met we felt that we were justified in assuming that basal conditions existed. Obviously, more than one test was necessary to accomplish this, but on the whole fewer readings had to be made than if the subjects were strangers to the environment and to the investigator. For the purpose of comparison of the pulse rate, blood pressure and basal metabolism and also of the basal metabolism and the values for blood cholesterol, the preliminary readings are included in the protocol at the end of the article. The lowest reading obtained in any of the tests was regarded as the basal rate for that subject. On occasions some factor such as illness prevented the test from being repeated on consecutive days, but this was of no consequence since the mentality of the children did not vary within such a short period of time.

The Benedict-Roth apparatus with a small rubber mouthpiece and an adaptable nose clip was used. The normal basal rates were calculated from the Harris-Benedict tables for boys and from the Talbot tables for girls, as suggested by Roth.[3] The blood pressure and pulse rate were noted during the tests. Blood for chemical analysis was drawn after the second basal reading so as not to upset the child emotionally. The children studied had recently been given intelligence tests based on the Stanford-Binet system by experienced psychologists employed by the institution. Errors in technic were decreased to a minimum by having one person (H. B. R.) conduct all the tests of the basal rate.

The analyses of the blood [4] were made by Mr. Haw, physiologic chemist, in the laboratories of the Michigan State Department of Health at Lansing. A twenty-four hour delay was caused by mailing the samples to the laboratory before the analyses were made. That very little error resulted from the blood's standing over night was shown by controls run on the same blood specimen on two successive days, which showed only a slight and negligible variation in the cholesterol and creatinine values.

There were ninety-eight subjects, fifty-nine boys and thirty-nine girls. These children were representative of the type found in the institution. They led essen-

3. Roth, P.: Personal communications to the authors.

4. The Myer-Wardell modification was used for determination of the blood cholesterol values. One cubic centimeter of blood measured with an Ostwald pipet, graduated to deliver, was thoroughly mixed in a small porcelain evaporating dish with 5 Gm. of plaster of paris. This mixture was dried for one hour at 95 F. in a water-jacketed drying oven. The dried material was then reduced to a powder of uniform consistency with a small agate pestle, which was transferred quantitatively to an extraction thimble and extracted with chloroform for one hour and one-half. The chloroform extract and washings of the extraction flask were made up to 25 cc. Ten cubic centimeters of the chloroform solution of the cholesterol was measured into a pyrex test tube and cooled in an ice bath for a few minutes. Two cubic centimeters of concentrated sulphuric acid was added, and the solution was mixed thoroughly by inverting the test tube and was placed in a beaker of water at 20 F. The green color was developed in the same light as that used in the colorimeter for a period of fifteen minutes, and the comparisons were made in the colorimeter immediately, the pure cholesterol standard solution being used with no more than three unknowns. The method of Folin and Wu was used for the determination of the creatinine after the precipitation of the proteins with tungstic acid.

tially normal lives, supervised by trained workers. The ages varied from 9.6 to 16 years in the boys and from 9.6 to 15 years in the girls. Among the former, the majority were between 12 and 14 years, while among the latter, the distribution was about the same in all ages. The intelligence quotients for both groups ranged between 60 and 120, most of them being between 70 and 100.

RESULTS

Charts 1 and 2 show that the basal metabolic rate was higher in the boys than in the girls. Of the boys, eight (13.5 per cent) had rates below zero, the lowest value being minus 9 per cent, in an epileptic patient; the rate in thirteen (22 per cent) was between 0 and plus 5; in twenty-five (42.4 per cent), between plus 5 and plus 10; in eleven (18.6 per cent), between plus 10 and plus 15, and in only one, above plus 15. This child was underdeveloped for his age and presented a clinical picture of facial lipodystrophy. A prepubertal rise was noted in some of the boys between the ages of 13 and 15 years.

Of the girls, nineteen (48.5 per cent) had rates below zero; in ten of these the rate was between 0 and minus 5 per cent, in seven between minus 5 and minus 10 and in two below 10, in one being minus 11 and in another minus 14. All these girls were normally developed, and free from disease except the last two, who showed signs or symptoms that were suggestive of thyroid deficiency. Among the remainder of the girls, the rate in seven (18 per cent) ranged from 0 to plus 5 per cent and in ten (25.6 per cent), from plus 5 to plus 10; in only three (about 8 per cent) was it above plus 10, being plus 18 in a rather nervous and unstable child. No prepubertal rise was observed.

Although the consensus has been that a low mental status is usually accompanied by a low basal metabolic rate, charts 3 and 4 tend to disprove such a conception. Here it is seen that there are as many metabolic rates above zero as below it in persons with subnormal intelligence, and the rates of all but eight of the boys were above zero, most of them being between plus 5 and plus 10 per cent. This indicates that there is no definite relationship between the mental status and the basal metabolism of a child. However, it is true that the intelligence quotients of the boys with metabolic rates below zero were 90 or less. This might have been a coincidence. It is noteworthy that of the girls, seventeen with minus metabolic rates had intelligence quotients varying from 70 to 95, whereas of those with intelligence quotients above this level only two had rates below zero as compared with nine who had rates above zero. That this is of little significance is shown by the remainder of the distribution. It intimates however that children with intelligence quotients over 95 rarely have low basal metabolic rates. This does not mean that those with intelligence quotients below 95 necessarily have low metabolic levels.

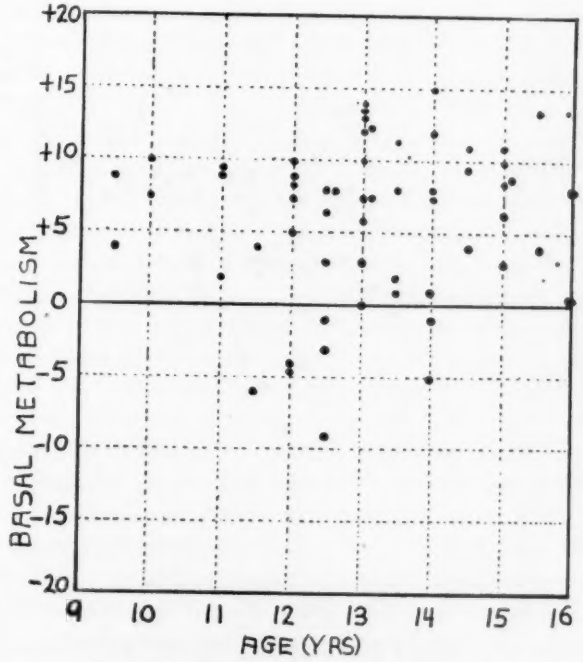

Chart 1.—The basal metabolism of the boys according to age.

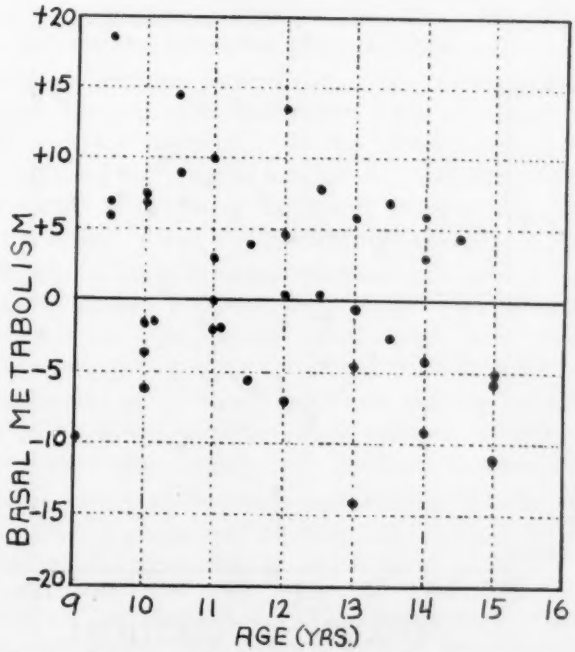

Chart 2.—The basal metabolism of the girls according to age.

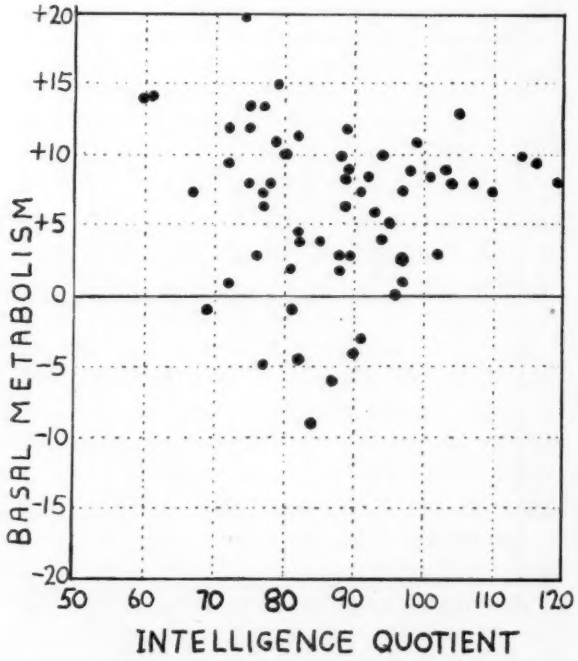

Chart 3.—The intelligence quotient and the basal metabolism of the boys.

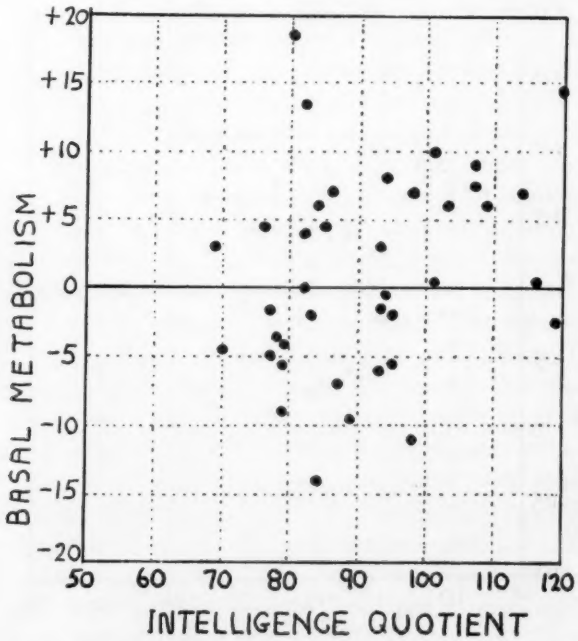

Chart 4.—The intelligence quotient and the basal metabolism of the girls.

Charts 5 and 6 show what relationship, if any, existed between the blood cholesterol and the basal metabolism of the group under study. Previous investigators have both proved and disproved the existence of any relationship. It has been suggested that a low basal metabolic rate is usually associated with a high blood cholesterol value and a high basal metabolic rate with a low cholesterol value, but not necessarily in an exact inverse ratio. My associates and I found approximately the same cholesterol values for children with high metabolic rates as for those with low basal rates, and in comparing the values for the same subject obtained on different days we noted variations which were on the whole independent of the rise or fall in the basal metabolic rate. The blood cholesterol values for the boys were somewhat lower than those for the girls, those for the majority ranging between 120 and 170 mg. per hundred cubic centimeters of whole blood. For the girls the values varied from 140 to 170 mg., a few being outside these limits. Recently, Gray and McGee [5] reported studies of the blood cholesterol on a group of feebleminded adults, finding the average content to be 154 mg. per hundred cubic centimeters of whole blood. There were no children in the group. A few subjects were between 15 and 20 years of age, and their rates were higher than in those of the older group. Considering 90 as the borderline quotient of normal intelligence, we found that in our group the boys with the quotients below the normal had an average cholesterol content of 153 mg. as compared with 152 mg. for the normal group. In the case of the girls the average for the normal group was 167 mg. and for the subnormal group, 155 mg.

The blood creatinine content was in most instances between 1.2 and 1.6 mg. per hundred cubic centimeters. The average for the boys was 1.37 mg. and for the girls, 1.33 mg., there being a slightly higher average for those with normal intelligence. The creatinine value seemed to be unrelated to the blood cholesterol value, to the basal metabolism and to the mental status of the individual child.

Although the blood pressure, the pulse rate and the basal metabolic rate usually showed a direct proportional relationship, this was not always true. On a number of occasions the blood pressure and the pulse rate were increased in spite of a lowered basal metabolic rate, and occasionally an increased pulse rate was not accompanied by an increase in the blood pressure. Roth [3] also noted that the pulse rate does not always vary directly with the basal metabolic rate.

Thirteen children, nine boys and four girls, showed evidence of simple adolescent goiter, and of these only one had an increased basal metabolic rate, the others having normal rates.

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5. Gray, H., and McGee, L. C.: Cholesterol Content of Blood in Epilepsy and in Feeblemindedness, Arch. Neurol. & Psychiat. **28**:357 (Aug.) 1933.

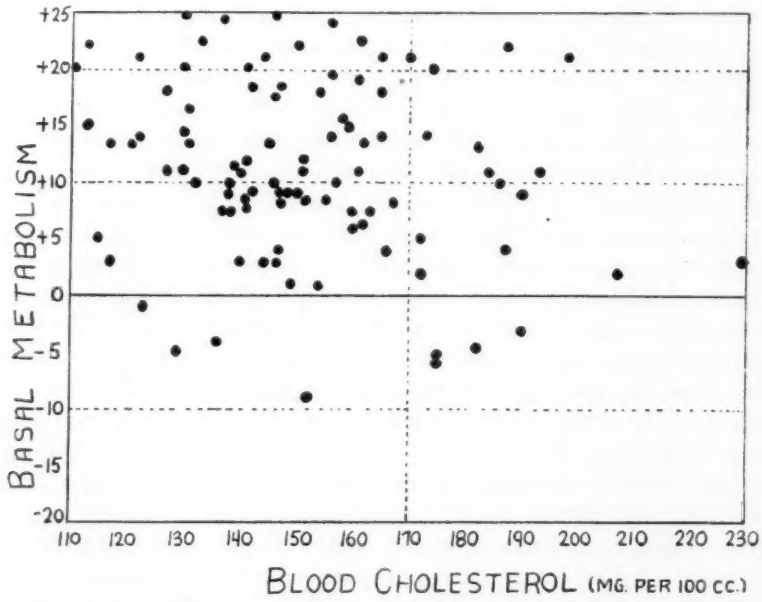

Chart 5.—The relationship between the blood cholesterol and the basal metabolism of the boys.

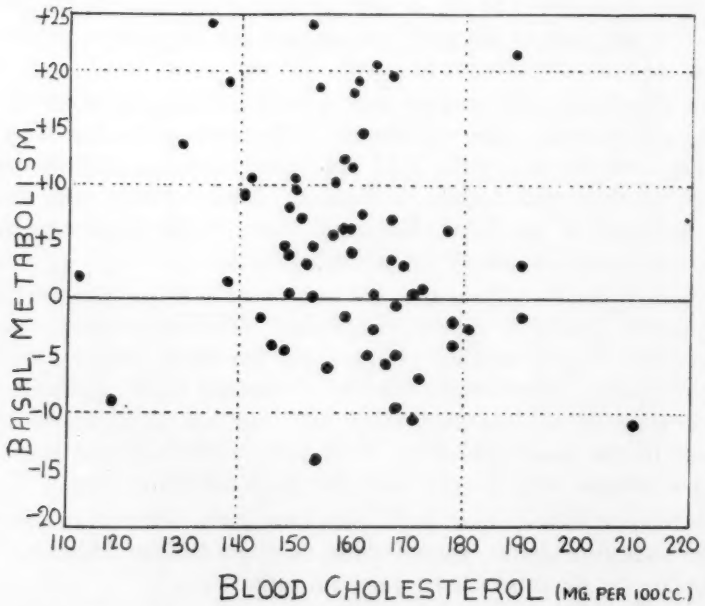

Chart 6.—The relationship between the blood cholesterol and the basal metabolism of the girls.

COMMENT

In estimating the metabolism of young persons [6] one should understand that one is dealing with growing tissue manifesting an increased cellular activity which is in turn dependent on the protoplasm and, to a less degree, on the less active fatty tissues. As the rate of cellular activity decreases so does the basal metabolic rate decrease. Such a sequence of events should explain the high basal rates noted in the boys in this series. However, the sequence does not fall in line with the lower basal rates found in the girls. What factors are responsible for this marked drop is difficult to ascertain, though it is known, and has been shown, that the basal metabolism of girls [7] and of women [8] is definitely lower than that of males of the same age groups. This might be explained on the basis of lessened functional activity.

Benedict [9] stressed the point that the basal metabolic rate is not to be regarded as inflexible and that deviations above or below the present standards should not be taken as abnormal. When one considers that in childhood the body is functioning at a higher rate than when growth and development decrease, a higher metabolic rate is to be expected, and its absence should make one suspect some disturbance in the function of the body. That values as high as plus 15 per cent are not unusual in a normal group of school children was demonstrated by Cameron,[10] who found the basal metabolic rate in 91 per cent of one hundred and forty-one children to be within the extreme normal limits of plus 15 and minus 15 per cent.

The question arises as to whether mental activity has any effect on the metabolism of the body. Lavoisier, in 1789, was probably the first to observe the influence of mental processes on the basal metabolic rate. He apparently believed that the metabolic rate increased with mental activity. Unfortunately he left no record of his experimental work. It was not until one hundred years later that interest was again aroused in this field, and since then thorough investigations have been conducted. Grafe [11] stated that the brain accounts for from 6 to 10 per

6. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Rep. 302, Carnegie Institution of Washington, 1921. DuBois, E. F.: The Basal Metabolism During the Period of Growth, Science **41**:567, 1915.

7. Talbot, F. G.: Disorders of Internal Secretion in Childhood, J. Pediat. **1**:769, 1932.

8. Cathcart, E. P., and Orr, J. B.: Discussion on Basal Metabolism, Brit. M. J. **2**:747, 1922.

9. Benedict, F. G.: The Basal Metabolism of Young Girls, Boston M. & S. J. **199**:127, 1923.

10. Cameron, A. T.: The Basal Metabolism in Two Hundred and Fifty Winnipeg Children, Canad. M. A. J. **15**:1022, 1925.

11. Grafe, E.: Ergebn. d. Physiol. **21**:412, 415 and 625, 1923.

cent of the total resting metabolism of the body. Benedict and Carpenter [12] studied twenty-two young men who were under mental strain during their regular collegiate examinations and found the metabolic rate in some of them to be the same or even lower during the examination than during the control periods, in spite of the fact that they were more nervous during the examinations. As a result of this investigation these workers concluded that mental effort does not produce any effect on the metabolism and expressed the opinion that if a rise occurs it is the result of the muscular movements associated with mental work. Speck [13] also found that mental activity has no bearing on the general metabolism. Becker and Olsen,[14] on the other hand, expressed the belief that the rise in the metabolic rate is parallel to the amount of mental work and that muscular movements accompanying mental effort account for only a fraction of this rise. However, they based their observations on the consumption of carbon dioxide, which according to DuBois [15] is not a reliable index under varying conditions.

Grabfield [16] and Bowman,[17] studying feebleminded adults, came to the conclusion that a low basal metabolic rate is the rule in persons in this condition. Banerji,[18] doing the same kind of investigation on a group of prisoners in a jail in Lucknow, noted that their basal rates were definitely lower, many being minus 10 per cent. Grafe and Trauman [19] observed that worry and anxiety caused a loss of weight, part of which they attributed to an increased metabolic rate. They demonstrated the effect of mental depression and excitation on a person in the hypnotic state and proved by their experiments that, except in a few instances of mental depression, the metabolic rate was raised. They explained this on the basis of emotional reaction. Landis [20]

12. Benedict, F. G., and Carpenter, T. M.: The Influence of Mental and Muscular Work on Metabolism, U. S. Dept. Agric. Office of Experiment Stations, bull. 208, 1909.

13. Speck: Arch. f. exper. Path. u. Pharmakol. **15**:81, 1882.

14. Becker, F. C., and Olsen, O.: Metabolism During Mental Work, Skandinav. Arch. f. Physiol. **31**:142, 1914.

15. DuBois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lea & Febiger, 1927, p. 408.

16. Bowman, K. M., and Grabfield, G. P.: Basal Metabolism in Mental Disease, Arch. Neurol. & Psychiat. **9**:358 (March) 1923.

17. Bowman, K. M., and Fry, C. C.: Basal Metabolism in Mental Disease, Arch. Neurol. & Psychiat. **14**:19 (Dec.) 1925.

18. Banerji, N. D.: Basal Metabolism of Prisoners of a District Jail in Lucknow, Indian J. M. Research **19**:229 (July) 1931.

19. Grafe, E., and Trauman, E.: Ztschr. f. d. ges. Neurol. u. Psychiat. **62**:237, 1920.

20. Landis, C.: Studies on Emotional Reactions and Metabolic Rate, Am. J. Physiol. **74**:188, 1925.

expressed the opinion that emotional disturbances or cumulative emotional upsets have no bearing on the metabolic rate. Our results indicate that the mentality of a child does not influence the basal metabolic rate, which is an individual entity and an individual expression of the functional level of the organism. Also I am inclined to agree with Landis for emotional disturbances in this group had less to do with a higher basal rate than the lack of practice in, and the discomfort of, breathing through the mouthpiece.

The relationship between the blood cholesterol and the basal metabolism opens another field for variation of opinion. Epstein and Lande [21] have shown that there is an inverse relationship between them. Bronstein,[22] in his interesting studies on cretins, demonstrated a high cholesterol value in his subjects with a subsequent fall to normal and an improvement in the clinical picture following thyroid therapy. He, however, did not claim that an inverse relationship exists. Mason, Hunt and Hurxthal,[23] while of the opinion that hyperthyroidism tends to diminish the level of cholesterol in the blood, nevertheless expressed the belief that there is no definite relationship. Grabfield and Campbell [24] and Gardner and Gainsborough [25] found no relationship. Although we were not dealing with cretins or with subjects with hyperthyroidism, the results substantiate the views of those who maintain that there is no definite relationship between the basal metabolism and the blood cholesterol.

Ward [26] carried out a series of studies on the cholesterol content of the blood with respect to age, using the Leiboff method, which compares well with the Myer-Wardell modification used by us. Ward's figures indicate a rise in the cholesterol value with an increase in age, with less rise in the values for girls than in those for boys. In her series of twenty-six boys from 6 to 13 years of age the values were between 125 and 145 mg. per hundred cubic centimeters of whole blood, and in the series of thirty-three girls from 8 to 12 years of age the

21. Epstein, A. A., and Lande, H.: Studies on Blood Lipoid, Arch. Int. Med. **30**:563 (Nov.) 1922.

22. Bronstein, I. P.: Studies in Cretinism and Hypothyroidism in Childhood, J. A. M. A. **100**:1661 (May 27) 1933.

23. Mason, R. L.; Hunt, H. M., and Hurxthal, L. M.: Blood Cholesterol in Hyperthyroidism and Hypothyroidism, New England J. Med. **203**:1273 (Dec. 25) 1930. Hurxthal, L. M.: Blood Cholesterol in Thyroid Diseases, Arch. Int. Med. **51**:22 (Jan.) 1933.

24. Grabfield, C. P., and Campbell, A. G.: Relation Between Blood Cholesterol and Basal Metabolic Rate, New England J. Med. **205**:1148 (Dec. 10) 1931.

25. Gardner, J. A., and Gainsborough, H.: Relationship of Plasma Cholesterol and Basal Metabolism, Brit. M. J. **2**:935 (Nov. 24) 1928.

26. Ward, K. M.: A Study of the Blood Cholesterol in Childhood, Arch. Dis. Childhood **6**:329 (Dec.) 1931.

Name	Age Yrs.	Age Mos.	Intelligence Quotient	Date	Basal Metabolic Rate	Temperature, F.	Pulse Rate	Blood Pressure	Cholesterol, Mg.	Creatinine, Mg.	Heat Production per Hour Normal	Heat Production per Hour Actual	Comment
Boys with Intelligence Quotients from 70 to 80													
C. S.	14	0	77	1/12/33	+21	98.6	60 - 60 - 60	90/60	.....	....	63.3	76.5	
				1/30/33	— 5[2]	97.6	50 - 54 - 60	90/68	129.0	1.43	64.6	61.4	
A. O.	12	7	72	11/23/32	+26	98.6	60 - 72 - 78	100/70	.....	....	53.4	67.5	
				2/17/33	+38	98.4	64 - 72 - 68	110/70	155.6	1.25	54.8	75.5	
				4/ 4/33	+22.5	98.0	68 - 68 - 76	100/60	161.2	1.43	55.6	68.2	
				4/ 5/33	+15.5	98.0	68 - 68 - 68	100/65	158.3	1.33	55.5	64.2	
				4/13/33	+12	97.8	64 - 68 - 64	100/65	.....	....	55.9	62.8	
B. R.	14	10	76	11/25/32	+ 6	98.6	78 - 78 - 78	100/70	.....	....	53.4	56.5	
				1/30/33	+ 3[2]	97.4	72 - 75 - 72	98/68	144.4	1.40	55.3	57.0	
W. B.	14	9	77	11/25/32	+11	98.6	78 - 72 - 84	120/90	.....	....	55.3	61.5	
				2/20/33	+ 6.5	98.0	64 - 68 - 68	110/75	161.2	1.28	55.7	59.5	
C. W.	14	4	72	11/25/32	+22	98.6	96 - 96 - 96	120/75	.....	....	58.8	72.0	
				1/26/33	+ 9.5	98.6	78 - 84 - 84	110/70	147.0	1.58	60.1	66.0	
J. Mc.	15	8	75	11/25/32	+ 8	98.6	78 - 78 - 78	100/70	.....	....	59.6	64.6	
				1/20/33	+15	98.0	72 - 72 - 75	100/70	112.6	1.42	61.3	70.5	
L. N.	15	0	77	11/29/32	+33	99.0	108 -104 - 96	100/70	.....	....	50.8	67.8	
				1/31/33	+22.5	98.2	90 - 78 - 92	118/70	133.4	1.38	52.7	64.6	
				3/29/33	+13.5	98.4	72 - 72 - 72	110/75	121.2	1.21	51.3	58.1	
D. B.	13	8	75	11/25/32	+14	98.6	60 - 57 - 60	100/60	.....	....	46.8	53.5	
				1/25/33	+12	98.4	56 - 57 - 59	105/68	151.0	1.15	48.1	54.8	
E. C.	13	4	79	11/25/32	+24.5	98.6	60 - 69 - 75	105/65	.....	....	52.7	65.6	
				1/25/33	+14	98.0	78 - 78 - 78	105/70	122.0	1.06	54.6	62.5	
				4/11/33	+20	97.6	68 - 72 - 72	100/65	.....	....	56.0	67.2	
				4/18/33	+17.5	97.2	64 - 68 - 68	95/65	.....	....	56.1	66.0	
				4/21/33	+15	97.2	68 - 68 - 80	.....	.....	....	56.1	64.8	
L. D.	12	9	75	11/28/32	+22.5	99.0	66 - 66 - 72	100/60	.....	....	60.7	74.5	
				1/28/33	+20	98.0	72 - 72 - 78	112/78	130.0	1.52	63.1	76.0	
				3/29/33	+13.5	98.0	72 - 76 - 80	120/80	144.8	1.33	65.9	74.5	
				4/11/33	+21	98.0	76 - 76 - 76	118/70	.....	....	66.2	80.0	
				4/15/33	+13.5	97.8	64 - 68 - 68	100/70	.....	....	66.5	75.4	
G. P.	11	10	77	11/29/32	+26	99.0	84 - 84 - 84	105/75	.....	....	44.6	56.5	
				1/29/33	+ 7.5	98.6	72 - 72 - 72	95/70	160.0	1.46	44.8	48.2	
H. R.	13	2	72	11/29/32	+13	98.6	72 - 72 - 66	110/70	.....	....	54.3	61.5	
				2/15/33	+ 1	98.0	72 - 72 - 76	110/70	153.8	1.47	55.4	55.7	
W. T.	13	11	69	11/29/32	— 1	98.4	66 - 66 - 66	100/70	.....	....	47.8	47.3	
				2/15/33	+ 4	98.4	60 - 60 - 66	96/68	147.0	1.34	48.3	50.4	

E. T.	13	0	67	11/30/32	+ 7.5	98.2	66 - 69 - 72	100/72	.....	....	45.5	49.0	
				2/16/33	+11	98.4	78 - 84 - 80	110/80	184.2	1.39	45.8	50.8	
D. W.	14	1	79	11/30/32	+45	98.4	94 - 94 - 84	130/75	.....	....	59.4	85.7	Congenital syphilis
				1/25/33	+26	98.8	78 - 90 - 93	120/80	130.0	1.03	61.7	77.5	
				3/30/33	+11	98.6	84 - 88 - 88	122/84	129.8	1.50	63.1	70.0	
L. W.	14	3	78	1/24/33	+ 8	98.4	84 - 81 - 84	112/78	141.0	1.28	46.7	50.6	Simple goiter
				2/ 1/33	+21	98.6	90 - 84 - 87	110/75	165.0	1.53	46.9	57.0	
C. C.	12	7	60	11/30/32	+17	98.0	78 - 78 - 78	105/70	.....	....	54.0	62.8	
				1/28/33	+19.5	97.6	72 - 84 - 84	120/70	156.0	1.13	53.8	64.2	
				3/31/33	+21	98.4	80 - 88 - 84	110/65	198.0	1.38	54.8	66.5	
				4/14/33	+14[2]	98.6	80 - 84 - 84	110/75	.....	....	55.0	63.0	
Boys with Intelligence Quotients from 80 to 90													
J. N.	15	2	80	11/18/32	+10	98.6	78 - 72 - 72	105/70	.....	....	68.0	75.0	
				1/31/33	+15.25	98.0	78 - 84 - 78	110/80	117.0	1.33	67.6	76.7	
V. G.	12	4	81	11/30/32	+18	98.0	69 - 66 - 72	100/70	.....	....	47.0	55.6	
				2/20/33	— 1[2]	98.2	60 - 64 - 72	100/70	122.6	1.47	45.9	45.4	
W. M.	11	5	87	12/ 1/32	+27.5	98.6	72 - 78 - 78	90/65	.....	....	45.5	57.5	Simple goiter
				2/20/33	— 6	97.6	60 - 64 - 60	100/70	175.4	1.43	46.7	44.0	
S. McW.	10	10	88	12/ 2/32	+13.5	98.6	69 - 72 - 78	105/70	.....	....	48.3	55.0	
				3/ 1/33	+22	97.6	88 - 84 - 85	110/70	186.8	1.44	48.2	59.0	
				4/ 4/33	+ 2	98.0	76 - 78 - 78	108/75	207.2	1.36	48.8	49.7	
R. T.	11	4	82	12/ 1/32	+ 4	98.6	78 - 84 - 87	110/70	.....	....	45.0	46.9	
				2/16/33	+11	98.4	76 - 76 - 80	110/75	139.8	1.20	45.1	50.0	
R. B.	12	9	89	1/10/33	+39	98.6	90 - 90 - 96	.....	.....	....	49.8	69.5	
				2/17/33	+17.5	98.6	84 - 88 - 84	120/75	146.4	1.27	49.2	58.0	
				3/31/33	+21	99.0	88 -100 - 96	118/75	170.0	1.41	49.1	59.4	
				4/15/33	+12[2]	98.6	80 - 84 - 88	115/70	.....	....	49.1	55.0	
G. K.	12	6	88	1/10/33	+ 5	98.6	72 - 72 - 72	118/80	.....	....	58.7	61.6	
				2/16/33	+ 3	98.4	64 - 64 - 64	118/80	117.0	1.44	60.2	62.5	
L. T.	12	4	89	12/ 3/32	+ 6.5	98.6	72 - 72 - 72	120/80	.....	....	52.1	55.6	
				2/17/33	+ 8.5	98.2	60 - 60 - 64	120/80	155.0	1.36	53.5	58.1	
D. D.	16	0	82	12/ 3/32	+ 4.5	98.0	66 - 66 - 66	120/75	.....	....	59.3	61.9	Bronchiectasis
				2/17/33	+ 5	98.0	64 - 68 - 68	110/80	115.0	1.33	60.0	63.0	Goiter
E. K.	14	3	85	12/ 6/32	+36	98.0	84 - 78 - 78	100/70	.....	....	47.8	65.0	
				2/16/33	+ 4	98.4	88 - 84 - 88	100/60	165.8	1.35	50.1	52.0	
J. R.	11	9	82	2/28/33	+ 3	98.6	88 - 88 - 96	105/75	235.2	1.55	54.2	56.0	Simple goiter
				3/ 6/33	— 4.5	98.0	84 - 92 - 84	110/85	181.6	1.35	54.4	52.0	
G. D.	10	6	84	11/25/32	+21	99.0	78 - 84 - 84	100/75	.....	....	42.5	51.5	Simple goiter
				2/ 1/33	+20	99.0	93 - 90 - 93	100/70	173.8	1.36	43.9	55.4	
				3/29/33	+26	98.8	88 -100 - 96	120/80	146.4	1.20	44.9	56.2	Facial lipodystrophy
				4/ 5/33	+23	98.6	84 - 92 - 88	110/70	.....	....	43.3	53.0	
				4/21/33	+23	98.6	84 - 88 - 93	110/75	.....	....	43.6	53.9	
				4/12/33	+40	99.0	72 -116 -106	110/75	.....	....	43.3	61.0	

Protocol—Continued

Name	Age Yrs.	Age Mos.	Intelligence Quotient	Date	Basal Metabolic Rate	Temperature, F.	Pulse Rate	Blood Pressure	Cholesterol, Mg.	Creatinine, Mg.	Heat Production per Hour Normal	Heat Production per Hour Actual	Comment
F. G.	13	1	82	12/ 3/32	+14	98.0	60 - 75 - 72	120/80	.....	....	62.0	70.5	
				2/16/33	+20	98.4	72 - 68 - 72	120/80	109.8	1.36	61.3	73.8	
				4/ 3/33	+11.5	97.8	64 - 72 - 72	120/80	139.4	1.35	64.8	72.2	
A. Y.	15	0	89	3/ 7/33	+ 8.5	98.0	57 - 64 - 63	90/65	140.8	1.45	61.9	67.0	
				4/ 4/33	+10	97.6	60 - 68 - 64	95/65	186.0	1.40	63.0	69.5	
E. N.	12	6	84	2/23/33	— 5.5	98.6	64 - 72 - 76	100/70	175.4	1.25	54.0	51.2	
				3/28/33	— 9	98.2	64 - 64 - 64	100/70	152.0	1.25	53.6	49.0	Epilepsy
R. H.	10	9	89	2/20/33	+ 9[2]	98.6	92 - 88 - 88	110/80	150.2	1.20	45.1	49.2	
				3/ 9/33	+11	98.2	68 - 64 - 64	100/65	151.4	1.46	45.2	50.4	
J. B.	13	5	81	3/ 1/33	+ 9	98.4	76 - 76 - 68	100/70	190.4	1.52	52.4	57.0	
				3/ 6/33	+ 2	98.0	76 - 76 - 84	95/70	171.6	1.43	52.7	53.6	
A. L.	12	8	88	2/22/33	+10	98.6	72 - 68 - 80	120/70	138.0	1.27	58.9	64.7	
				3/20/33	+11	98.2	64 - 60 - 64	110/80	132.4	1.44	59.2	65.9	
L. W.	13	2	89	2/22/33	+14	98.0	72 - 80 - 72	118/80	156.0	1.35	53.6	61.2	
				3/21/33	+ 3	98.0	72 - 68 - 72	100/75	139.8	1.36	53.9	55.5	
						Boys with Intelligence Quotients from 90 to 100							
C. S.	12	9	96	12/ 1/32	+22	98.0	63 - 63 - 75	115/70	.....	....	51.2	62.5	Simple goiter
				2/20/33	+12	98.2	60 - 60 - 64	115/68	141.4	1.22	52.2	58.4	
				4/13/33	+ 0[2]	97.4	60 - 56 - 52	100/70	.....	....	54.0	54.0	
W. H.	13	0	93	12/ 3/32	+18	98.0	72 - 66 - 75	120/85	.....	....	64.6	76.0	
				2/ 1/33	+ 6	97.8	72 - 78 - 72	120/80	160.0	1.38	65.8	69.5	
C. F.	14	4	92	12/ 6/32	+28	98.0	81 - 90 - 84	140/85	.....	....	67.4	86.2	
				2/20/33	+18.5	98.6	78 - 84 - 84	125/75	147.0	1.25	70.6	83.7	
				3/30/33	+13.5	98.2	80 - 88 - 80	110/70	138.4	1.82	72.0	81.7	
				4/12/33	+ 8.5	97.4	73 - 68 - 70	110/70	.....	....	72.3	78.5	
R. K.	11	7	94	2/21/33	+10	98.6	76 - 84 - 80	100/70	156.8	1.35	46.2	51.0	
				3/24/33	+ 9.5	98.4	76 - 76 - 76	90/60	148.0	1.46	46.1	50.5	
D. K.	12	1	98	2/22/33	+18.5	98.6	88 - 84 - 88	120/70	142.0	1.47	55.2	65.5	
				3/20/33	+ 9	98.4	72 - 68 - 72	100/70	141.8	1.43	56.1	61.1	
W. E.	12	0	90	3/ 1/33	+20	98.4	76 - 84 88	110/75	140.8	1.46	53.3	63.8	Simple goiter
				3/ 7/33	— 4[2]	98.6	76 - 84 - 80	105/80	136.0	1.29	53.1	51.5	
J. M.	11	10	95	2/21/33	+14	98.6	68 - 72 76	90/65	164.6	1.25	51.4	58.5	
				3/ 8/33	+ 5	98.6	56 - 64 - 64	88/60	172.4	1.29	51.4	54.2	
J. B.	14	0	97	3/ 2/33	+11.5	98.0	68 - 73 - 72	110/70	150.8	1.65	65.8	73.5	Simple goiter
				3/28/33	+ 1	99.0	76 - 76 - 76	110/70	149.2	1.46	66.2	66.6	

G. B.	12	5	91	2/23/33	— 3	98.2	68 - 72 - 68	105/70	190.4	1.15	51.0	49.5	
				3/22/33	+14	98.2	64 - 68 - 72	115/70	173.0	1.57	50.9	58.0	
L. D. S.	15	4	94	2/28/33	+11	97.8	76 - 84 - 72	98/74	193.2	1.41	55.4	61.5	Simple goiter
				3/ 7/33	+ 4[2]	97.8	68 - 72 - 72	98/70	186.8	1.40	55.4	57.1	
H. I.	14	11	99	2/21/33	+21	97.2	68 - 64 - 68	105/75	121.8	1.32	60.0	72.6	
				3/21/33	+11	97.6	68 - 66 - 78	100/70	127.4	1.48	60.0	66.5	
				4/13/33	+14	98.0	60 - 60 - 64	90/70	.....	....	61.1	69.5	
N. V.	14	2	97	3/ 2/33	+14.5	97.8	56 - 60 - 64	110/75	129.8	1.38	61.6	70.7	
				3/ 8/33	+ 7.5	97.6	56 - 60 - 68	105/65	136.6	1.35	62.1	64.4	
W. N.	13	2	91	2/24/33	+ 7.5[3]	98.0	72 - 72 - 72	110/80	138.0	1.43	65.4	70.2	
				3/24/33	+16.5	98.2	80 - 72 - 76	95/60	130.8	1.36	66.2	77.0	
Boys with Intelligence Quotients of 100 or More													
R. M.	13	3	105	2/28/33	+13	98.8	100 - 88 - 84	120/80	181.8	1.54	57.1	64.7	
				3/ 7/33	+13.5	98.4	72 - 72 - 72	120/65	161.8	1.33	57.3	65.0	
P. M.	9	1	103	10/13/32	+20.5	98.2	84 - 93 - 84	110/70	.....	....	44.2	53.5	
				3/ 6/33	+15	98.0	84 - 80 - 80	90/60	158.6	1.24	45.8	54.0	
				4/ 3/33	+22	98.4	68 - 76 - 84	100/70	150.2	1.33	45.7	56.0	
				4/14/33	+16	98.6	92 - 92 - 88	95/60	.....	....	46.0	53.4	
				4/18/33	+ 9	97.6	72 - 72 - 76	96/65	.....	....	46.3	50.5	
P. F.	10	2	114	3/ 3/33	+22	98.4	92 - 92 - 88	110/75	112.6	1.30	43.9	53.5	
				3/ 9/33	+10	98.4	76 - 80 - 76	96/65	145.8	1.33	43.8	48.4	
R. W.	10	1	110	3/ 3/33	+24.5	98.0	68 - 72 - 72	110/70	137.0	1.36	48.4	60.2	
				3/ 9/33	+ 7.5[2]	98.0	68 - 72 - 68	95/68	163.2	1.36	48.4	52.0	
R. S.	10	9	116	2/27/33	+18	98.2	88 - 88 - 84	115/70	153.8	1.44	46.8	55.1	
				3/22/33	+ 9.5	98.4	80 - 80 - 84	95/60	138.0	1.49	46.9	51.2	
A. C.	11	8	101	2/27/33	+ 8	99.0	80 - 80 - 88	100/60	166.6	1.60	50.1	54.1	
				3/22/33	+ 8.5	98.2	68 - 82 - 72	85/55	150.8	1.45	50.2	54.5	
T. L.	12	6	107	3/ 3/33	+21	98.0	76 - 80 - 84	110/80	144.4	1.32	56.1	68.0	
				3/ 8/33	+18	97.8	84 -100 - 96	130/80	165.2	1.41	56.1	66.0	
				4/ 3/33	+38	98.6	88 - 96 -100	.....	144.8	1.40	55.9	77.0	Emotional
				4/14/33	+ 8[2]	97.4	80 - 80 - 80	120/80	.....	....	55.8	60.4	
L. W.	12	4	119	2/24/33	+ 8	98.6	88 - 84 - 80	110/70	147.0	1.32	60.1	67.6	
				3/23/33	+13.5	98.2	80 - 72 - 76	95/60	130.8	1.36	60.0	65.0	
J. H.	13	2	104	2/24/33	+24	98.6	88 - 84 - 90	140/70	156.0	1.33	60.2	75.0	
				3/23/33	+19	98.2	80 - 88 - 96	140/80	161.2	1.29	60.4	72.0	Tense
				4/12/33	+17	98.6	80 - 80 - 80	130/80	.....	....	61.0	71.5	
				4/15/33	+ 8	98.2	70 - 68 - 80	120/75	.....	....	60.9	65.5	
T. S.	9	6	102	2/27/33	+11	98.8	84 - 80 - 68	100/75	161.2	1.49	48.7	54.3	
				3/24/33	+ 3	98.4	63 - 60 - 68	98/68	146.4	1.26	49.2	50.7	
Girls with Intelligence Quotients from 70 to 80													
I. H.	14	0	69	5/ 5/33	+13.5	98.4	68 - 68 - 68	105/65	.....	....	52.5	59.5	Malnutrition
				5/12/33	+ 3	98.7	64 - 68 - 64	115/70	190.0	1.34	52.8	54.4	
N. B.	13	5	76	4/24/33	+12	98.4	68 - 72 - 76	120/80	158.6	1.46	52.0	58.2	
				5/ 3/33	+ 7[2]	97.6	60 - 64 - 64	90/65	167.2	1.41	52.1	55.6	

Protocol—Continued

Name	Age Yrs.	Age Mos.	Intelligence Quotient	Date	Basal Metabolic Rate	Temperature, F.	Pulse Rate	Blood Pressure	Cholesterol, Mg.	Creatinine, Mg.	Heat Production per Hour Normal	Heat Production per Hour Actual	Comment
H. B.	14	0	79	4/24/33	+ 2	98.0	88 - 88 - 92	112/80	112.1	1.33	57.5	58.6	
				5/17/33	— 9	97.6	76 - 80 - 76	98/70	117.6	1.28	57.5	52.4	Acne
R. B.	14	6	79	1/13/33	+13	98.0	84 - 78 - 84	110/75	.....	....	58.5	66.5	
				4/28/33	— 5.5	98.6	64 - 64 - 68	110/70	167.2	1.46	58.5	55.5	
B. D.	13	10	76	10/13/32	+19	99.0	120 -108 -102	120/78	.....	....	52.5	61.3	Coryza
				5/ 1/33	+20.5	98.8	76 - 76 - 88	115/70	163.8	1.36	56.5	68.2	
				5/16/33	+ 4.5	99.0	81 - 80 - 96	130/80	152.6	1.50	55.5	58.1	
E. C.	9	8	78	1/13/33	— 3.5	98.2	78 - 72 - 75	90/60	.....	....	44.0	42.4	
				4/26/33	+ 1.5	97.6	60 - 68 - 64	90/58	138.4	....	46.8	47.6	
L. P.	10	1	77	5/ 2/33	+ 3	98.2	84 - 88 - 88	105/75	152.0	1.23	49.2	50.8	
				5/15/33	— 1.5	98.0	76 - 88 - 84	105/80	157.4	1.23	49.3	48.5	
D. H.	13	8	74	5/17/33	+10.5	97.8	92 - 92 - 96	110/70	149.8	1.27	51.7	57.2	Simple goiter
				5/23/33	+ 6	98.6	80 - 76 - 80	108/75	158.6	1.24	52.1	55.2	
B. C.	15	0	77	5/ 4/33	+ 2	99.0	76 - 72 - 80	125/80	.....	....	60.7	61.9	
				5/11/33	— 5	99.0	84 - 76 - 80	125/75	168.4	1.33	60.7	57.5	
H. C.	14	3	79	5/ 4/33	— 1.5	98.0	72 - 68 - 72	118/78	.....	....	60.5	59.5	
				5/11/33	— 4	98.4	64 - 64 - 68	100/65	177.6	1.42	60.5	58.0	
H. C.	13	0	70	5/ 9/33	— 4	98.4	72 - 72 - 76	100/70	145.8	1.20	54.2	52.0	
				5/15/33	— 4.5	98.6	76 - 76 - 82	120/85	148.0	1.36	54.2	51.7	
Girls with Intelligence Quotients from 80 to 90													
V. D.	10	10	85	1/17/33	+11	98.6	66 - 78 - 78	105/70	.....	....	42.5	47.1	
				4/26/33	+ 4.5	99.0	72 - 68 - 68	105/70	147.6	1.18	43.5	45.5	
M. R.	11	0	82	4/27/33	— 0.5[2]	98.6	80 - 84 - 80	105/75	153.2	1.29	46.5	46.3	
				5/ 3/33	+10	98.8	72 - 72 - 72	105/65	157.4	1.36	45.6	50.4	
H. B.	11	4	82	4/27/33	+ 4	98.0	96 -100 -108	105/70	160.0	1.23	42.7	44.6	
R. V.	12	9	84	5/18/33	—10.5	97.8	64 - 64 - 56	100/70	170.8	1.40	64.0	57.2	Lethargic
				5/29/33	—14	98.6	60 - 56 - 56	90/65	153.8	1.36	63.2	54.4	
R. D.	11	10	87	5/ 2/33	— 5	98.0	80 - 84 - 76	105/70	163.2	1.30	46.2	43.8	
				5/11/33	— 7	97.8	80 - 80 - 80	95/60	172.4	1.24	46.9	43.7	
L. H.	9	6	80	5/ 2/33	+18.5	98.8	96 -104 -104	100/70	144.4	1.33	47.3	56.0	
				5/16/33	+19	98.6	96 -108 - 96	110/70	151.4	1.43	47.5	56.6	
				6/ 3/33	+27	98.6	84 - 72 -100	116/80	.....	....	47.7	60.5	
C. H.	11	8	82	5/17/33	+19	98.6	88 - 84 - 85	118/80	138.0	1.38	48.5	57.6	
				5/29/33	+13.5	99.0	76 - 92 - 88	120/80	130.2	1.46	48.5	55.1	
R. F.	8	9	89	5/18/33	— 9.5	98.6	80 - 72 - 84	100/65	168.4	1.33	42.9	38.9	
				5/23/33	+ 1	98.6	80 - 76 - 72	95/68	172.4	1.23	43.3	43.6	

J. H.	12	4	84	5/31/33	+10.5	99.0	88 - 92 - 96	120/80	141.8	1.32	45.2	50.0	Malnutrition
				6/ 7/33	+19.5	98.7	108 -104 -100	118/80	156.6	1.33	45.6	54.5	
				6/12/33	+ 8	99.0	88 - 96 - 92	122/80	.....	....	45.5	49.2	
M. M.	9	9	88	5/ 4/33	+14.5	99.0	126 -112 -112	105/75	.....	....	41.2	47.2	
				5/16/33	+ 7	98.8	96 -104 -100	125/80	150.8	1.58	41.6	44.6	
C. B.	11	3	83	5/29/33	+ 5.5	98.0	88 - 96 - 86	140/80	156.8	1.25	55.0	58.0	
				6/12/33	— 2	98.6	88 - 96 - 96	130/80	.....	....	54.5	53.4	
Girls with Intelligence Quotients from 90 to 100													
I. B.	11	0	93	1/17/33	+14	98.6	84 - 72 - 72	98/70	.....	....	47.2	54.0	Simple goiter
				4/26/33	+ 3	98.6	64 - 68 - 68	90/60	169.4	1.21	48.0	49.5	
L. T.	14	8	98	1/17/33	+ 1	98.4	90 - 92 - 90	118/78	.....	....	58.7	59.5	Lethargic
				4/27/33	—11	98.0	72 - 76 - 80	95/65	210.4	1.54	59.3	53.2	No menses
				6/ 8/33	— 2.5	98.6	80 - 80 - 84	105/70	163.8	1.21	59.2	57.9	Treatment with thyroid, 1 grain (0.06 Gm.) daily
R. J.	9	11	93	5/ 3/33	+ 4.5	98.7	76 - 76 - 80	108/70	149.2	1.30	48.5	50.6	
				5/12/33	— 1.5	98.0	84 - 84 - 85	105/70	144.4	1.31	49.0	48.4	
M. N.	12	3	94	10/14/32	— 3	98.6	72 - 66 - 84	115/80	.....	....	56.5	54.2	
				5/18/33	— 0.5	98.4	68 - 68 - 68	105/70	168.0	1.46	59.9	59.6	
S. B.	11	5	95	5/19/33	— 5.5	98.6	80 - 80 - 80	110/70	.....	....	51.7	48.7	
				5/31/33	+ 0.5	98.4	76 - 80 - 76	110/70	149.2	1.28	51.7	52.0	
G. G.	13	2	99	5/22/33	+ 6[2]	98.0	54 - 51 - 57	105/70	176.8	1.65	59.2	62.7	
				6/ 1/33	— 8[2]	98.0	60 - 56 - 60	115/75	149.2	1.46	59.2	63.8	
B. C.	9	10	93	5/22/33	+11.5	98.7	72 - 76 - 76	112/80	160.0	1.52	50.1	55.9	
				6/ 1/33	— 6	97.6	68 - 76 - 68	110/75	156.0	1.20	50.5	47.5	
D. G.	9	6	93	6/ 2/33	+ 9.5	98.0	72 - 64 - 66	105/75	150.2	1.36	45.6	50.0	
				6/ 7/33	+ 6	98.6	76 - 76 - 80	100/70	160.0	1.48	45.6	48.5	
G. T.	10	7	97	6/ 2/33	+24.5	99.0	96 -112 -104	115/70	135.2	1.33	38.4	47.7	Malnutrition
				6/ 7/33	+ 9	98.9	96 -108 - 93	100/70	141.4	1.39	38.8	42.2	
F. H.	10	9	95	6/ 2/33	+21.5	99.0	84 - 80 - 80	108/80	188.6	1.31	42.8	52.0	
				6/ 8/33	— 2	98.6	72 - 68 - 68	110/80	178.2	1.25	42.5	41.5	
I. M. L.	9	7	97	10/12/32	+ 9	98.6	96 - 84 - 84	88/65	.....	....	40.7	44.4	
				6/ 5/33	+ 7.5	98.6	84 - 80 - 84	105/78	161.8	1.25	42.8	46.6	Malnutrition
L. W.	11	10	91	1/17/33	+10	98.2	96 - 96 - 96	95/70	.....	....	39.6	43.5	Simple goiter
				5/31/33	+18	98.0	80 - 80 - 80	98/65	150.2	1.27	41.6	49.1	
Girls with Intelligence Quotients of 100 or More													
E. J.	9	9	122	10/11/32	+15	98.6	78 - 78 - 78	100/70	.....	....	39.2	45.1	
				6/ 5/33	+14.5	98.2	80 - 80 - 72	110/75	161.8	1.25	42.9	49.0	Aggressive
A. J.	11	9	116	10/11/32	+ 5.5	98.0	66 - 66 - 66	100/70	.....	....	52.5	55.5	
				6/ 5/33	+ 0.5	98.2	64 - 60 - 63	105/75	172.0	1.40	57.0	57.2	
V. C.	12	0	101	5/22/33	+ 3.5	98.6	76 - 76 - 72	95/70	166.6	1.46	50.0	51.4	
				6/ 1/33	+ 0.5	98.2	84 - 80 - 76	95/75	163.8	1.33	50.0	50.3	
I. H.	13	4	119	6/ 6/33	— 1.5	98.0	72 - 72 - 72	110/80	190.4	1.45	59.7	59.0	Acne
				6/ 8/33	— 2.5	98.0	72 - 72 - 64	100/70	180.8	1.28	59.4	58.0	
V. R.	9	7	114	6/ 6/33	+24	99.0	112 -102 -105	130/80	153.2	1.28	45.2	56.1	Simple goiter
				6/12/33	+ 7[2]	98.6	88 - 92 - 88	118/80	.....	....	46.0	49.1	

values were from 125 to 157 mg. The values for the group reported on here were somewhat higher than those for Ward's group, and there was a tendency toward lower levels in the boys. Furthermore, we did not observe an increase in the value for blood cholesterol with an increase in age. A search through the literature did not reveal any studies on the blood creatinine with respect to the basal metabolic rate. Our work did not disclose any connection between them.

CONCLUSIONS

1. There was no definite relationship between the basal metabolic rate and the intelligence quotient (as determined by the Stanford-Binet tests) in the group of children studied.

2. The basal metabolic rate was definitely lower in the girls.

3. The normal basal metabolic rate of boys may be placed between minus 10 and plus 15 per cent, and of girls, between minus 10 and plus 10 per cent. The metabolic rate in boys may be as high as plus 15 per cent without abnormality being discoverable.

4. The blood cholesterol and creatinine values did not seem to correlate with the basal metabolic rate. The cholesterol level was slightly lower in the boys.

5. There was no essential difference in the blood cholesterol values for subjects of normal and those of subnormal mentality.

SUMMARY

Ninety-eight children were studied, fifty-nine boys and thirty-nine girls. The intelligence quotients varied between 60 and 120.

The basal metabolic rate in the boys ranged between minus 10 and plus 15 per cent, and in the girls, between minus 15 and plus 15 per cent. There were two subjects, one boy and one girl, whose basal rates were higher.

The blood cholesterol values for the boys varied between 120 and 170 mg. per hundred cubic centimeters and for the girls, between 140 and 170 mg. The average for the boys of normal and subnormal mentality was 153 mg. In the case of the girls the average for the subnormal group was 155 mg. and for the normal group, 167 mg.

The blood creatinine level ranged between 1.2 and 1.6 mg. per hundred cubic centimeters. The average for the boys was 1.37 mg. and for the girls, 1.33 mg.

The blood pressure and pulse rate in the majority of instances were directly proportional to the basal metabolic rate.

BIRTH PAINS AND THE BLOOD OF THE NEW-BORN

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Every investigator of the cause of icterus neonatorum agrees that immediately after birth the number of red blood corpuscles and the hemoglobin index are high and that these values decrease for a few hours after birth. After the second or third day these values steadily decrease until the normal physiologic levels are reached. The great destruction of red blood cells that occurs during the decrease leads to the large accumulation of bile pigment in the blood stream which is the direct cause of the jaundice.

REVIEW OF THE LITERATURE

Lénárt [1] was the first to note that the pains of labor greatly influence the behavior of the red blood cells in the fetus. According to his theory the chorionic villi are injured during labor, and through these injuries the maternal iso-agglutinin and isohemolysin enter the fetal blood stream, where by iso-agglutination and isohemolysis the red blood cells are destroyed. After this destruction, the original high number of cells is further decreased until the red blood cell count and the hemoglobin index reach normal physiologic values.

Adler [2] also noted a relationship between birth pains and the blood of the fetus. According to him, if the fetus is brought into the world at the beginning of labor by means of a cesarean operation the bile pigment content of the blood in the umbilical cord is not increased—that is, if the birth pains are absent, hyperbilirubinemia does not take place.

Hoffmann and Anselmino [3] also called attention to the importance of the part played by the birth pains in producing an increase in the number of red blood cells. Their explanation for this increase is that under the influence of the birth pains the carbon dioxide content of the fetal blood is greatly increased, which in turn leads to a decrease in

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1. Lénárt, G.: Orvosi hetil. **72**:830, 1928.
2. Adler, K.: Arch. f. Gynäk. **144**:586, 1931.
3. Hoffmann, F., and Anselmino, R. J.: München. med. Wchnschr. **79**:1226, 1932.

the oxygen pressure, the direct result of which is an increase in the number of red blood cells. The investigators did not attach much importance to this occurrence.

According to Adler [2] the increase of the bile pigment in the blood of the new-born (hyperbilirubinemia) is due to the effect of the birth pains on the fetus, and the hyperbilirubinemia is attributed to hemolysis which occurs as the result of the birth pains.

Horváth,[4] of the obstetric clinic of the University of Szeged, stated that jaundice rarely occurs in the infants who are brought into the world by means of a cesarean operation. This, however, does not furnish the reason for the absence of the increase of the bilirubin content in the blood stream in the cases in which cesarean operation is performed. The question of whether the absence of hyperbilirubinemia is due to the increase of the red blood cells (polycythemia) or to a morphologic change in the blood was not answered.

METHODS OF INVESTIGATION

The definite aim of our study was to seek a solution of these problems. All of the available data dealing with the increase of the bile pigment content in the blood of the new-born were carefully studied, since these observations were to be the starting-point of our investigation.

We estimated the number of red blood cells and the hemoglobin index of eighteen mature and of twelve premature infants. We compared the results with those obtained from eight mature infants delivered by means of a cesarean operation. In each of the last group of infants the removal from the uterus occurred at the very beginning of labor, even before the uterus had opened. Immediately after birth, blood taken from the umbilical artery, the umbilical vein and the heel was examined. Blood was taken hourly: two, four, six, eight, twelve, eighteen and twenty-four hours after birth and then daily; the specimen was taken at the same time on each day and always from the same heel. The results are shown in table 1.

RESULTS AND COMMENT

Of the eighteen mature infants, the smallest weighed 2,800 Gm. and the largest, 4,000 Gm. Immediately after birth we estimated the number of red blood cells as 4,500,000 and the hemoglobin index as 88 per cent. At this time the number of red blood cells was 11 per cent greater, and the value of the hemoglobin index, 16 per cent higher, in blood obtained from the umbilical artery than in that from the umbilical vein (red blood cells, 4,500,000; hemoglobin index, 88 per cent). A comparison of the results of examination of the blood from the heel

4. Horváth, Z.: Magyar orvosi nagyhet. jegyzókönyve, 1932.

and from the umbilical vein showed in the former an increase of 20 per cent in the number of red blood cells and of 25 per cent in the hemoglobin index. Two hours after birth the peak of the increase was reached; at this time the number of red blood cells had increased 39 per cent and the hemoglobin index, 46.5 per cent. From this point the number of red blood cells and the hemoglobin index steadily decreased until they reached normal physiologic levels.

Of the twelve premature infants the smallest weighed 1,620 Gm. and the largest, 2,500 Gm. The number of red blood cells in blood

TABLE 1.—*Average Postnatal Red Blood Cell Count and Hemoglobin Index for Eighteen Mature and Twelve Premature Infants and for Eight Infants Delivered by Cesarean Operation*

	Mature Infants		Premature Infants		Infants Delivered by Cesarean Operation: Expansion of Uterine Orifice of 1 Inch		Infants Delivered by Cesarean Operation: Expansion of Uterine Orifice of 2 Inches	
	Average Number Red Blood Cells*	Hemoglobin Index, per Cent	Average Number Red Blood Cells*	Hemoglobin Index, per Cent	Average Number Red Blood Cells*	Hemoglobin Index, per Cent	Average Number Red Blood Cells*	Hemoglobin Index, per Cent
Blood from								
Umbilical vein	4.500	88	4.120	84	4.390	88	4.300	91
Umbilical artery	5.010	102	No examination		No examination		No examination	
Heel	5.420	110	5.040	103	4.390	88	4.670	102
After birth								
2 hours	6.250	129	5.330	111	4.990	95	5.300	112
6 hours	5.890	119	5.500	118	4.810	98	5.800	119
12 hours	5.890	120	5.700	118	4.680	89	5.200	113
2 days	5.660	109	5.220	106	4.440	88	4.900	97
3 days	5.460	110	5.500	107	4.450	87	5.030	99
4 days	5.590	114	5.220	106	4.450	90	4.670	97
5 days	5.340	107	5.200	100	4.460	88	4.900	103
6 days	5.290	104	5.160	99	4.550	85	5.170	103
7 days	5.400	110	5.150	95	4.470	90	4.900	102
8 days	5.330	105	4.970	92	4.300	85	4.800	99
9 days	5.260	106	4.910	92	4.410	84	4.600	96
10 days	5.170	105	4.860	90	4.300	82	4.700	95
11 days	5.100	102	4.770	89	4.300	82	4.600	88

* The number of red blood cells is expressed in millions.

taken from the umbilical vein was 4,100,000; the hemoglobin index, 84 per cent. Examination of blood from the umbilical artery was omitted. Blood taken from the heel immediately after birth showed an increase of 20 per cent in the number of red blood cells and of 22.5 per cent in the hemoglobin index above the values obtained from examination of blood from the umbilical vein. Twelve hours after birth the values reached their highest point, which represented an increase of 38 per cent in the number of red blood cells and of 40.5 per cent in the hemoglobin index. From this time the decrease in the values was steady until normal physiologic levels were reached.

Of the eight cases of cesarean operation we found in five an expansion of the external uterine orifice of 1 inch (2.5 cm.). In the remain-

ing three cases the expansion was 2 inches (5 cm.). The average number of red blood cells in the blood of the umbilical vein of the infants in the five cases in which the uterine orifice showed an expansion of 1 inch was 4,300,000, and the hemoglobin index, 88 per cent. Again no examination was made of the blood taken from the umbilical artery. The values for the blood taken from the heel proved to be the same as those found for the blood from the umbilical vein. At the end of the first hour after birth we found no increase in either the number of red blood cells or the hemoglobin index. The increase really began in the second hour after birth, at which time, in fact, the height of the increase occurred. This peak was 13.5 per cent for the red blood cell count and 11 per cent for the hemoglobin index.

On examination of the blood from the umbilical vein of the infants in the three cases in which the external uterine orifice showed an expansion of 2 inches, we found the number of red blood cells to be 4,300,000 and the hemoglobin index, 88 per cent. In the blood taken from the heel we found an increase of only 8.5 per cent in the number of red blood cells and of 12 per cent in the hemoglobin index. The summit of the increase was reached six hours after birth; the peak showed an increase of 35 per cent in the red blood cell count and 31 per cent in the hemoglobin index. From this point, the values decreased steadily until the normal physiologic levels were reached.

Besides the eight infants delivered by cesarean operation we examined two others in whose mothers an expansion of the external uterine orifice of 3 inches (7.62 cm.) was noted. The values obtained differed but slightly from those of infants with a normal birth.

We extended our investigations to the cases in which abortions were necessary. The blood from twelve immature living fetuses was examined. An average of 3,500,000 red blood cells was found; the hemoglobin index was 72 per cent.

It is evident from the results cited that at the moment of birth the fetus, depending on the degree of maturity, enters the world with a certain hemoglobin index as well as a certain number of red blood cells. The values which are characteristic of the new-born are much higher than those of immature infants. Comparison of the values obtained from an immature infant with those from an adult reveals that the former values are lower. In mature infants the number of red blood cells and the hemoglobin index are practically the same as in the adult. In some cases the values are even greater. During the early postnatal period there is a steady increase in the number of red blood cells and in the hemoglobin index, but in the cases in which cesarean operation was necessary before the pains of labor appeared the increase both in the number of red blood cells and in the hemoglobin index was barely noticeable. We were able to determine the difference in the number of

red blood cells and in the hemoglobin index between the blood from the placenta and that from the heel. In cases of natural birth there was a difference of 20 per cent in the number of red blood cells and of 25 per cent in the hemoglobin index. In the cases in which an expansion of the external uterine orifice of 2 inches was noted, the difference was only 8 per cent and 10 per cent, respectively. In cases in which the expansion was only 1 inch, no proportional difference was found, and the increase in the number of red blood cells and in the hemoglobin index began one hour after birth. This circumstance strengthens the supposition that the characteristic, determinable proportional increases are due to the changes activated by the pains of labor, since in cases of cesarean birth the increase begins only two or three hours after birth. Immediately after natural birth in which the labor pains were not absent,

TABLE 2.—*Red Cell Count and Hemoglobin Index of the Placental and Fetal Blood in Four Cases of Immature Birth*

	Month of Fetal Life							
	Fourth		Seventh		Ninth		Ninth	
	Red Blood Cells*	Hemoglobin Index, per Cent	Red Blood Cells*	Hemoglobin Index, per Cent	Red Blood Cells*	Hemoglobin Index, per Cent	Red Blood Cells*	Hemoglobin Index, per Cent
Placental blood	No examination		No examination		3.600	81	3.200	84
Fetal blood	2.300	58	No examination		No examination		No examination	
1 hour after birth	No examination		4.500	114	No examination		3.200	84
2 hours after birth	No examination		No examination		3.600	81	No examination	
3 hours after birth	No examination		No examination		No examination		3.200	84

* The number of red blood cells is expressed in millions.

a decided increase in the number of red blood cells and in the hemoglobin index was found, the increase being attributed to the effects of the labor pains.

We were unable to determine the reason for the differences between the values for the placental and those for the fetal blood. In order to clear up this question, the manner in which the labor pains affect the blood must first be known. The results of our investigations lead us to the supposition that the values obtained from the placental blood correspond to those which are to be found in the fetal blood prior to the period of birth. This supposition is strengthened by the results obtained from the investigation of four cases in which surgical assistance was necessary owing to the serious condition of the mother. Of the four births, one was immature and three premature. We were unable to perform complete examinations owing to the quick death of the fetus. The results are given in table 2.

In table 2 it may be seen that the values obtained from the placental blood are the same as those obtained from the fetal. In each case

labor pains were absent. It is also of interest that the values did not change, even three hours after birth. We may conclude, therefore, that had the infants lived, the increase either would not have occurred or would have been of slight degree.

Schiff,[5] Elder and Hutchinson attributed the increase in the number of red blood cells in the early postnatal hours to a drying-out process brought about by the large loss of fluid. According to our investigations, the part played by this drying-out process involves cases of natural birth as well as cases in which cesarean operation is necessary. In the cases in which cesarean removal is necessary prior to the beginning of labor pains, the increase in the number of the red blood cells and in the hemoglobin index may be attributed to this drying-out process. In the cases in which the birth was natural or surgical intervention was preceded by the labor pains, the increase is due to the changes brought about by these pains.

We observed all of the necessary precautions in taking the blood for the examinations. At the time of taking the blood, the infant was placed flat on the stomach, and each of us took blood from each heel. Working independently, we made the necessary examinations and then compared our results. We took for the final value the mean of the separate results, provided a difference of 200,000 in the red cell count and of 5 per cent in the hemoglobin index was not exceeded. If this occurred new counts were made.

SUMMARY

1. The number of red blood cells and the hemoglobin index of the blood of the intra-uterine fetus is not greater than that of the adult.

2. At the moment of birth the number of red blood cells is increased, and the hemoglobin index is greater. The changes are due to the effect of the pains of labor. A few hours after birth the height of the increase is reached, which represents an average value of 40 per cent. This result is in agreement with those of other investigators.

3. The degree of increase is dependent on the time required for the birth. A minor part is played by the drying-out process, which tends to thicken the blood.

5. Schiff, E.: Jahrb. f. Kinderh. **34**:159 and 459, 1892; **54**:1 and 172, 1901.

STUDIES IN IMMUNITY

V. EFFECT OF ACUTE DISEASES ON THE REACTION OF THE SKIN TO TUBERCULIN

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CINCINNATI

From previous studies [1] it was concluded that there is a depression of the local skin reaction to tuberculin during the acute stage of certain infections. Observations were continued so that statistical evaluation could be made.

In the first article,[1a] in 1928 reference was made to the medical literature. Since then a number of reports on the nonspecific effect of conditions other than tuberculosis on the reaction to tuberculin have appeared in the literature. Many of these record such a small number of observations and are so inconclusive that they hardly warrant quotation. Debré [2] concluded from his study of 229 children that the anergic effect of measles on the reaction to tuberculin was greater the more marked the rash and the higher the temperature. Lereboullet and Baize [3] observed 16 persons who gave a positive skin reaction to tuberculin. During measles 14 showed a depression of skin sensitivity to tuberculin, which in 9 instances was observed from twenty-four to thirty-six hours before the eruption. The anergy tended to disappear about the sixth or seventh day of the disease. Caraffa [4] noticed a difference in sensitivity to the Pirquet and Mantoux methods of testing with tuberculin during the paroxysmal stage of pertussis, particularly when it was complicated

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1. (*a*) Mitchell, A. G.; Wherry, W. B.; Eddy, B., and Stevenson, F. E.: Studies in Immunity: Nonspecific Factors Influencing Reaction of Skin to Tuberculin, Am. J. Dis. Child. **36**:720 (Oct.) 1928. (*b*) Eddy, B., and Mitchell, A. G.: Studies in Immunity: Effect on Skin Tuberculin Reaction of Nonspecific Factors, Am. J. Dis. Child. **40**:771 (Oct.) 1930.

2. Debré, R.: Sur la disparition de la cuti-réaction positive à la tuberculine pendant la rougeole, Arch. de méd. et pharm. mil. **87**:521 (Oct.) 1927.

3. Lereboullet, P., and Baize, P.: Rougeole et cuti-réaction tuberculinique, Arch. de méd. d. enf. **34**:701 (Dec.) 1931.

4. Caraffa, C.: Contributo clinico allo studio dell'allergia tubercolinica nelle diverse fasi della pertosse, Clin. pediat. **14**:935 (Dec.) 1932.

by bronchopneumonia. When the reaction to the Pirquet test was negative, a positive reaction to the Mantoux test was obtained. Depression of the skin reaction to tuberculin has been observed in typhoid [5] and in typhus [6] and during reactions to phenyl-ethyl-hydantoin.[7] Rosenthal [8] and Martenstein,[9] on the assumption that only about 20 per cent of adults with mycosis fungoides gave positive reactions to tuberculin, expressed the belief that this disease exerted an anergic influence on tuberculin tests. In three proved cases of active tuberculosis associated with lymphogranulomatous lesions of the neck Nobécourt, Martin and Liège [10] were unable to secure a positive reaction to tuberculin. No evidence of tuberculosis could be demonstrated in the lymphogranulomatous lesions at necropsy. Parker, Jackson, Fitzhugh and Spies [11] obtained fewer positive reactions to tuberculin in patients with diseases of the lymphoid and myeloid tissues and in those with malignant disease than they did in normal persons and in tuberculous patients. The depressive effect of ultraviolet and roentgen rays on the reaction to tuberculin has been noted by several observers.[12] Hausmann and

5. Garibbo, A.: Il comportamento della cutireazione alla tubercolina nell'infezione tifoide dei bambini, Ann. d. inst. Maragliano **8**:31 (Jan.-Feb.) 1931.

6. Wu, C. J., and Reimann, H. A.: Effect of Typhus Fever on Intracutaneous Tuberculin Reaction, Nat. M. J. China **17**:210 (April) 1931.

7. Tezner, O.: Die Beeinflussung der Pirquetschen und Schickschen Probe durch das Nirvanolexanthem, Monatschr. f. Kinderh. **47**:409, 1930.

8. Rosenthal, S. K.: Beiträge zur Kenntnis der exfoliativen generalisierten Erythrodermien: Erythrodermische Form der Mycosis fungoides (nebst Bemerkungen über die Tuberkulinanergie bei M. f.), Arch. f. Dermat. u. Syph. **164**:82, 1931.

9. Martenstein, H.: Zur Tuberkulinanergie bei Mycosis fungoides. Beitrag zu vorstehender Arbeit von Dr. S. K. Rosenthal, Arch. f. Dermat. u. Syph. **154**: 198, 1927.

10. Nobécourt, P.; Martin, R., and Liège, R.: Recherches relatives à la tuberculose chez trois enfants atteints de lymphogranulomatose maligne, Arch. de méd. d. enf. **36**:73 (Feb.) 1933.

11. Parker, F., Jr.; Jackson, H., Jr.; Fitzhugh, G., and Spies, T. D.: Studies of Diseases of Lymphoid and Myeloid Tissues: Skin Reactions to Human and Avian Tuberculin, J. Immunol. **22**:277 (April) 1932.

12. Lautmann: Action des U.V. sur la cuti-réaction à la tuberculine, Ann. Inst. d'actinol. **2**:298 (July) 1928. Genoese, G.: L'influenza della luce solare sulla cutireazione alla tubercolina, Policlinico (sez. prat.) **35**:1343 (July 16) 1928. Nasta, M.; Jovin, I., and Blechmann, M.: Diminution de la sensibilité à la tuberculine chez le cobaye tuberculeux soumis à l'irradiation par les rayons X, Compt. rend. Soc. de biol. **100**:906 (April 8) 1929. Muggia, A.: Influence des rayons ultra-violets sur la réaction de la peau à la tuberculine, Acta pædiat. **11**:67, 1930. Clauser, F.: Contributo allo studio dell'azione biologica dei raggi Röntgen; irradiazione röntgen e cutireazione alla tubercolina umana, Riv. di radiol. e fis. med. **2**:493 (Oct.) 1930. Bratusch-Marrain, A., and Asperger, H.: Ueber den Einfluss von Ultravioletttbestrahlung auf die Pirquet- und die Schickreaktion, Med. Klin. **28**:1310 (Sept. 16) 1932. Storchi, L.: Influenza dei raggi ultravioletti sulla cutireazione alla tubercolina, Pediatria **37**:416 (April 15) 1929.

Fisher [13] found that irradiation of the tuberculin decreased the local skin reaction in man and in guinea-pigs and the general reaction in guinea-pigs. Engel [14] submitted experimental evidence which he contended demonstrated that the so-called seasonal variation in tuberculin allergy depend on the type of diet.

METHOD OF STUDY

This study was carried out in the wards of the department for contagious diseases of the Cincinnati General Hospital. We had knowledge of the skin response to tuberculin in some of the subjects before the onset of the acute contagious disease, since we had performed these tests on children who, prior to admission to the wards for contagious diseases, had been in the Children's Hospital, the pediatric department of the General Hospital, the Children's Convalescent Home of the Cincinnati Orphan Asylum, the Preventorium of the Hamilton County Tuberculosis Sanatorium or one of several orphanages. Koch's old tuberculin and bovine tuberculin were used in doses of 0.1 mg. in 0.1 cc. of an 0.85 per cent solution of sodium chloride. Later, old tuberculin was used in the same dosage, but 0.0005 mg. of human tubercule bacillus protein in 0.1 cc. of an 0.85 per cent solution of sodium chloride was employed in the place of the bovine tuberculin. Combined with the figures obtained in the latest study are those of two previous ones [1] in which human and bovine tuberculin were used. In all of these studies the same type and the same dosage (unless otherwise stated) of tuberculin were employed in the same patient before, during and after the acute period of his disease.

There was only 1 instance in which the reaction to bovine tuberculin was positive when the reaction to old tuberculin was negative, and only 1 in which the reaction to bovine tuberculin was larger than that to old tuberculin. The results of the tests with human tubercle bacillus protein are not used in this study for the determination of the rates of reactions. Intracutaneous injection was the method employed in all instances. Only those reactions which were at least 1 cm. in diameter and which were elevated above the surface of the skin forty-eight hours after the injection were considered positive. The tests were repeated during convalescence, as a rule from three to four weeks after the onset of scarlet fever and pertussis and approximately two weeks after the onset of measles, diphtheria and mumps. After the initial test, readings were made daily for several days and in many instances for as long as three weeks. The test made during convalescence was read daily for from two to six days.

INTERPRETATION OF RESULTS

It is apparent from the observations noted in table 1 that a depression of the cutaneous response in persons normally giving a positive reaction is produced by the acute stage of certain diseases. From a statistical standpoint there is significance in the difference between the rates of reaction obtained during the febrile and during the convalescent stage

13. Hausmann, W., and Fischer, A.: Ueber Lichtwirkung auf Tuberkulin, Strahlentherapie **41**:750, 1931.

14. Engel, P.: Der Einfluss der Ernährung auf die jahreszeitlichen Schwankungen der Tuberkulinallergie, Arch. f. Dermat. u. Syph. **167**:279, 1933.

of scarlet fever. While the difference between the rate during the febrile and that during the convalescent stage of measles is significant, it is too close to the threshold to merit emphasis. It is possible that the rate of reaction during convalescence would have been higher if the tests on patients with measles had been made later than two weeks after the acute stage of the disease. In diphtheria, while the rate in both the febrile and the convalescent stage is stable, there is no significant difference between the rates, which from a statistical point of view argues that diphtheria does not affect the skin response to tuberculin.

TABLE 1.—*Depression of the Skin Response During the Acute Stage of Diseases in Persons Normally Giving Positive Reactions to Tuberculin*

		Positive Reaction to Tuberculin Test				
		Febrile Stage		Convalescent Stage		
Disease	Number of Cases	Number	Rate, Cm.	Number	Rate, Cm.	$\frac{K}{PE_K}$
Scarlet fever.....	854	35	0.041 ± 0.007	179	0.210 ± 0.014	10.88
Measles.....	283	19	0.067 ± 0.015	50	0.177 ± 0.023	4.04
Diphtheria.....	140	16	0.114 ± 0.027	27	0.192 ± 0.033	1.83
Miscellaneous....	210	12	0.057 ± 0.016†	23	0.110 ± 0.022	.....
Poliomyelitis..	38	3		3		
Varicella.....	57	4		12		
Pertussis.....	79	3		3		
Mumps.....	4	0		0		
Other diseases.	32	2		5		
Total.....	1,487	82	0.055 ± 0.006	279	0.188 ± 0.010	11.29

* In the formula $\frac{K}{PE_K}$, K equals the difference between the rates of reaction in the febrile and in the convalescent stages, and PE_K equals the probable error of this difference. When $\frac{K}{PE_K}$ is greater than 4, it is statistically significant. For example, the result 10.88 indicates that the chances are about seventy billion to one that the difference between the rates of the skin reaction to tuberculin in the acute and convalescent stages of scarlet fever is not due to chance. On the other hand, for diphtheria $\frac{K}{PE_K}$ is 1.83, indicating that a difference as great, or greater than this, would arise by chance alone approximately twenty-five of one hundred times without the operation of any causal factor, this not being regarded as statistically acceptable proof that it might not be a chance phenomenon.

† This is not a stable rate.

The number of observations on individual diseases considered in the miscellaneous group is too small to give stable rates.

The depression in the tuberculin skin reaction is, in practically all instances, quantitative and partial, since during the acute stage of certain diseases the positive reaction obtained is almost invariably smaller than the reaction present during convalescence. For example, in 29 cases in which the reaction was positive during both stages the mean size of the reaction in the acute stage was 1.96 ± 0.14 cm. and during convalescence, 3.93 ± 0.28 cm. $\frac{K}{PE_K}$ equaled 6.35, showing a significantly greater mean size during convalescence.[15]

15. The mathematical significance of the formula $\frac{PE_K}{K}$ is fully explained in the footnote to table 1.

In a previous study [1b] it was found that by increasing the dosage of tuberculin during the acute stage a positive reaction could sometimes be obtained when a smaller dose failed to elicit a response. Furthermore, the reaction may be delayed during the acute stage but be quickly positive when the test is made during convalescence. In table 2 are shown 38 instances in which the reaction to tuberculin became definitely positive, although only after several days.

The reaction may not only be delayed but may be affected in degree. In table 3 are shown 12 comparative measurements of the size of the

TABLE 2.—*Delayed Positive Reactions to Tuberculin*

Day After Injection on Which Reaction Became Positive	Number of Reactions
4	10
5	6
6	8
7	6
8	1
9	1
10	2
11	1
13	1
14	2
Total	38

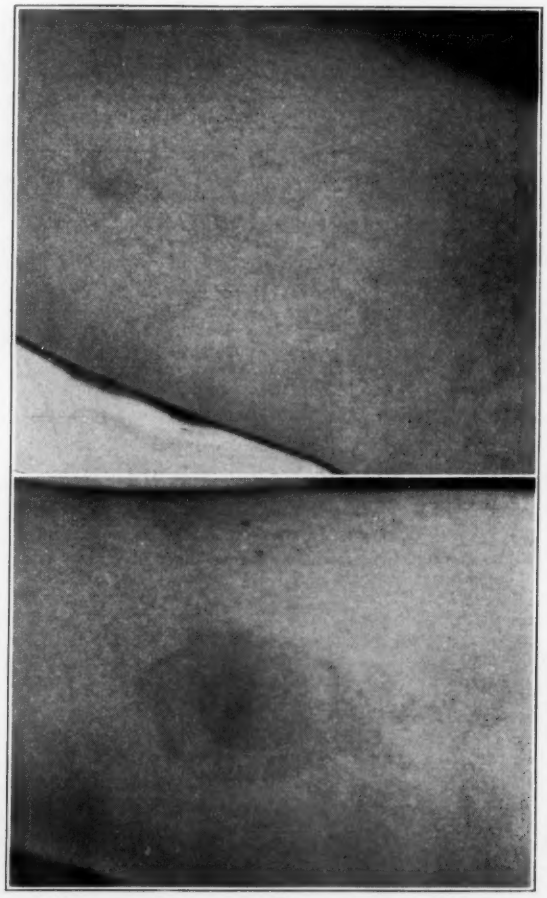
TABLE 3.—*Comparative Measurements of Delayed Reactions*

Small Delayed Reactions—Less than 1 Cm.	
Day on Which Reaction Became Positive	Number
5	1
7	1
8	1
9	1
10	2
11	1
12	2
14	1
15	2
Total	12

reaction during the febrile stage and during the convalescent stage. The mean size of the initial reaction was 0.54 ± 0.04 cm., but in each instance it was much larger during convalescence, the mean being 3.78 ± 0.35 cm. $\frac{K}{PE_K}$ equaled 9.21, showing that the size was significantly greater during convalescence. Such reactions are illustrated in the accompanying photograph.

It seems proper to question whether the amount of tuberculin used in the initial skin test was sufficient to bring about sensitization to tuberculin and thus cause the skin reaction later to become positive or to be increased in size. The number of cases in which we knew the tuberculin reaction before, during and after the acute febrile stages

of the various diseases was insufficient for statistical analysis. However, there were 9 children who within a few months before the onset of measles gave a positive reaction to tuberculin. Of these, 3 gave negative reactions during the febrile stage of measles, but all 9 again gave positive reactions during convalescence. There were 10 cases of scarlet



The upper figure shows delayed reaction to tuberculin during the acute stage of scarlet fever. The first appearance was on the fourteenth day after the injection. The height of the reaction (0.6 by 0.7 cm.) was reached on the fifteenth day. The lower figure shows the reaction as it appeared during the convalescent stage, twenty-nine hours after the injection of tuberculin.

fever in which the tuberculin reaction was positive within a few months before the onset of the disease. In 4 of these it became negative, but in all 10 the reaction was positive during convalescence. An additional argument against the possibility of sensitization as the cause of initiat-

ing or increasing a response to tuberculin is that the rate of positive reactions to tuberculin obtained during convalescence in this group of patients is not excessively high as compared with our own studies on normal children tested for the first time. For example, in 729 children who received injections of tuberculin for the first time, the number of positive reactions was 127 and the rate was 0.174 ± 0.014, as compared with the rate of 0.188 ± 0.01 of our convalescent group. $\frac{K}{PE_K}$ equaled 0.775, showing that there was no significant difference between these rates. We have also compared the mean size of the reactions in a group of children tested for the first time with the mean size of the reaction in our convalescent group. In the former the mean size was 3.02 ± 0.09 cm. and in the latter, 2.56 ± 0.11 cm. Here $\frac{K}{PE_K}$ was 2.48, showing that there is no significant difference between these sizes. In other words, this is a further indication that previous injection of tuberculin does not increase the size of the reaction to later injections. It should be stated, however, that in certain instances when the retest was made during convalescence there were very small reactions (less than 1 cm. in diameter and with little or no edema) which appeared within twenty-four hours and which faded in forty-eight hours. The frequency of such reactions was important only after the injection of old tuberculin and human tubercle bacillus protein. Thus, 51 of 88 patients in one group with scarlet fever treated in this manner gave no reaction to the initial test but gave small reactions which faded rapidly after the second test, in contrast to only 13 such reactions in 236 patients of another group tested with old tuberculin and bovine tuberculin. Since these reactions were so slight and faded so rapidly, it can be stated that any of the definitely positive reactions (greater than 1 cm. in diameter and elevated above the surface of the skin) could hardly have been the result of sensitivity induced by previous injections of tuberculin.

In only 1 instance did a child who had failed to give a reaction to tuberculin prior to admission to the wards for contagious diseases give a definitely positive reaction during the convalescent stage. The first test on this patient was made eight months before the onset of measles. At the time of the latter observation he had tuberculous spondylitis.

Although we feel confident that we have not confused our results by obtaining positive reactions during convalescence after the previous injection of tuberculin, we are not prepared to say that sensitivity to tuberculin cannot be created by the injection of tubercle bacillus protein. This does not seem to be possible to a significant degree when either human or bovine tuberculin or both are employed in the ordinary amounts used for skin testing. However, the evidence just cited of the greater frequency of small, rapidly fading reactions observed after the simultaneous use of old tuberculin and human tubercle bacillus

protein suggests that a low-grade sensitivity to tuberculin may be induced by the use of these two tuberculins. Furthermore, in a study now in progress on a group of normal children we obtained these small fleeting reactions, although there was no cutaneous response on the first injection of tuberculin.

CONCLUSIONS AND SUMMARY

A depression of allergy to tuberculin exists during the acute stages of scarlet fever, and probably of measles, which disappears during the convalescent stage. This is shown: (1) by significant differences in the occurrence of positive reactions during the acute and during the convalescent stage; (2) by the depression of allergy in persons known to give positive reactions; (3) by a delay in the time of the appearance of the reaction during the acute stage, and (4) by the smaller size of the skin reaction in the acute stage as compared with that in the convalescent stage.

From a practical clinical standpoint it follows that failure to elicit a skin response to tuberculin during the acute stage of scarlet fever, and probably of measles, cannot be accepted as evidence that the person does not normally give a positive reaction.

No statistically significant difference can be demonstrated between the rates of positive reaction to tuberculin during the acute and convalescent stages of diphtheria. This is the more conclusive since stable rates of reaction were obtained for both the acute and the convalescent stage of the disease.

Case Reports

LYMPHOGRANULOMA INGUINALE

WITH RECTAL MANIFESTATIONS IN A CHILD

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This is a report of a case of lymphogranuloma inguinale in an 8 year old girl, who showed only rectal symptoms. The diagnosis was confirmed by a positive reaction to a Frei intradermal test.

Although there is extensive literature regarding the disease in adults, no case has been reported in childhood. It has been stated:[1] "That it is a venereal disease cannot be doubted; it is not seen in children and always follows sexual exposure."

REPORT OF A CASE

History.—M. M., an 8 year old girl, a Puerto Rican, came to the United States when 1 year old. The mother, aged 30, had lymphogranuloma inguinale with rectal stricture. The disease first manifested itself in the mother in 1921, while she was in Puerto Rico. At that time she suffered from enlargement and suppuration of the left inguinal nodes, in addition to vaginal discharge. For two years previous to the birth of the patient the mother complained of rectal symptoms which were caused by the development of a tight rectal stricture. This necessitated a colostomy, which was performed in 1928 in the United States. She had a persistently positive Frei reaction. The father gave a history of unilateral suppurative inguinal adenitis twelve years previously. A Frei test on the father gave a positive reaction. A sibling died at the age of 6 years from an unknown infection.

The patient was born in Puerto Rico, at full term, and delivery was spontaneous. No cyanosis, convulsions, rash or snuffles was evident. There were no congenital anomalies. The child was breast fed exclusively for two months and gained weight steadily. There were no difficulties in feeding throughout early infancy. The child's development was normal. She sat up at the age of 5 months, had the first tooth at the age of 8 months and walked at the age of 1 year. At the age of 3 years the child contracted scarlet fever, with no apparent complications. Two months later she was treated at Bellevue Hospital, New York, for a vaginal discharge. There was no adequate proof that the vaginitis was specific,

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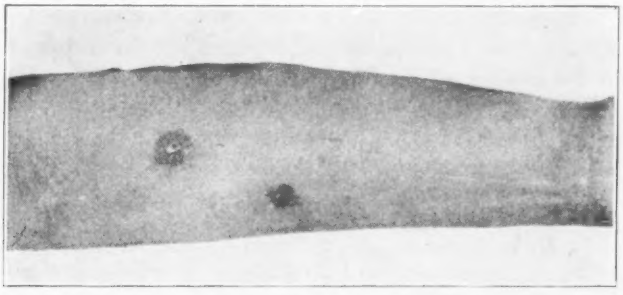
1. De Wolf, H. F., and Van Cleve, J. V.: Lymphogranuloma Inguinale, J. A. M. A. **99**:1065 (Sept. 24) 1932.

since the smears were inconclusive for gonococci. She had chickenpox at the age of 3½ years. At the age of 6 she had measles without complications. There was no history of smallpox, rheumatic fever, cholera or pertussis. She was vaccinated against smallpox and received diphtheria toxin-antitoxin at the age of 3 years. At 7 years of age a tonsillectomy was performed because of frequent colds.

The patient was well until four weeks prior to admission to the hospital, when she passed a few drops of bright red blood with every bowel movement. Gross amounts of blood disappeared from the stool in one week, but mucus continued to be present at all times. She began to complain of severe tenesmus. Her appetite was good at all times. No dietary limitations were imposed. No loss of weight was noticed. The child was brought to the outpatient clinic because of tenesmus and rectal bleeding and was then admitted to the pediatric service of Mount Sinai Hospital. Because of the history of her mother's infection a Frei test was done which gave positive results. Control tests made simultaneously on normal persons gave negative reactions. The test was repeated on the patient, a different known antigen being used, and again gave positive results. In addition, chiniofon-casein was used both on the patient and on the controls. In all cases the reaction was negative.



Reactions to injections of 0.1 cc. of Frei antigen. The upper papule shows the appearance after five days, and the lower one, the appearance after forty-eight hours.

There is no history of rectal trauma or abnormal sexual contacts. The child was accustomed to sleep in the same bed with her mother, and on many occasions bathed in the same tub with her mother. A common cloth was often used for washing and drying by the mother and the patient. A rectal tip used by the mother was employed in giving enemas to the child.

Physical Examination.—The patient was a well developed, well nourished child, not acutely ill. The skin was clear except for a small herpetic lesion on the right cheek. A few inguinal and axillary nodes were palpable, but were not large or tender. Vaginal examination revealed an intact hymen and no vaginal lesions or discharge. All other physical observations gave normal results except those referable to the rectum. On inspection a small fissure was seen above the external anal sphincter to the right of the midline posteriorly.

Proctoscopy revealed a fold of mucous membrane in the rectum, 6 cm. from the anal margin. The fold was edematous. An irregular, superficial ulceration of the mucous membrane was seen, which at its most prominent point measured 1 cm. by 5 mm. The surface was granular and bled easily. The picture gave an impression of subacute ulcer. On the left lateral wall was a flat, circular ulcer,

which did not bleed. This measured about 5 mm. in diameter. A small, flat ulcer was seen posteriorly. This was circular, had a grayish, granular base and did not bleed.

The urinalysis gave negative results. The blood smear showed no abnormal cells. The blood count showed: red cells, 4,900,000; white cells, 7,300; polymorphonuclears, 54 per cent; lymphocytes, 36 per cent; eosinophils, 9 per cent, and monocytes, 1 per cent. The Wassermann reaction was negative. A smear from the stool was negative for amebas and ova, and the guaiac test gave negative results. On culture the stool showed Bacillus coli. The Pirquet, Mantoux and Schick tests gave negative reactions. A vaginal smear failed to show gonococci.

Course and Therapy.—During her stay in the hospital the child was isolated. A bland diet was ordered. Repeated injections of Frei antigen were given in an effort to establish immunization. She received ten intradermal injections. These were given into the skin of the forearms in 0.1 cc. doses at three day intervals. All injections were followed by local reactions typical of a positive Frei reaction. This consisted of a persistent erythematous skin papule about 4 mm. in diameter surrounded by an erythematous halo measuring 1.5 cm. The patient complained of localized itching at the sites of the injections, but there were no systemic reactions. The reactions were all uniform; the reaction to the last injection resembled in every way the reaction to the first one, as shown in the accompanying photograph. The patient was given no local treatment by rectum. Her bowel movements remained normal and contained no blood. Repeated proctoscopic examinations revealed progressive healing at the sites of the ulcerations. After treatment for two weeks the largest ulceration was entirely healed and the others were less acute in appearance. At the end of three weeks proctoscopic examination revealed complete healing of all the rectal ulcerations. Two months later proctoscopic examination revealed recurrent ulcerations at the sites of the original lesions. The mucous membrane up to 6 cm. above the anal margin was granular and edematous. Bleeding from the rectum was noted on several occasions. These observations persisted until the last examination of the child in November 1934.

CLINICAL PICTURE

Lymphogranuloma inguinale is a chronic infectious process which involves the genitalia or neighboring parts and shows little or no tendency to spontaneous healing. In 1913 Durand, Nicolas and Favre [2] related the disease to venereal contact. The disease starts with a primary lesion which is a solitary superficial erosion, the size varying from that of a pinpoint to that of a pea. It is usually situated on the surface of the prepuce or in the sulcus coronarius of the glans penis in the male, and in the female on the cervix, in the vagina at the fourchet or on the labium minus. The initial lesion has also been found in the urethra and on the neck, on the tongue and on the fingers. A physician became infected on the finger while operating on a patient with a disturbance in the inguinal glands of unknown origin. The

2. Durand, M.; Nicolas, J., and Favre, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **35**:274 (Feb. 6) 1913.

axillary glands of the physician went through the typical course seen in lymphogranuloma inguinale. Twenty-three years later Hellerström obtained a positive Frei reaction from this patient.

Characteristic of the initial lesion is its small size, its nonpainful nature and its evanescent character. The incubation estimated by Hellerström [3] varies from ten to thirty days. Men were thought to be affected much more frequently than women. However, this seems to apply more to the involvement of the inguinal nodes, and the difference may not be so great if the anorectal localization is included, which is seen most often in women, with little or no accompanying inguinal adenitis. That the anorectal syndrome occurs almost exclusively in women is due to the anatomic difference in the lymphatic drainage from the initial lesion. The disease apparently is seen most often in young adults. In a group of fifty-eight cases, the average age was 27 years, the youngest patient being 19 years old.[1]

In men the drainage from the genitalia involves the superficial inguinal glands. These glands become swollen, hard and tender. They fuse to the skin, which assumes a reddish-violet hue. Later, multiple areas of softening may appear and eventually break down, producing multiple fistulous openings. The deep iliac lymph nodes in the pelvis may become involved secondarily. In men the flow of lymph from the penis and scrotum may be impeded by the firm retractile scarring, so that elephantiasis of these parts may follow. When the fibrotic scarring of the perirectal lymphatics is extensive, a rectal stricture may be the inevitable consequence.

In women it is the exception for the inguinal adenopathy to become manifest. The lymph drainage from the clitoris and external vulva passes into the inguinal nodes, whereas the supply from the vaginal mucosa and especially from the posterior vaginal wall drains into the lymph nodes around the rectum, where there are three lymph plexuses extending up into the rectum to a height of from 4 to 6 cm.

The infection of the plevic lymph nodes in women leads to inflammation, which has a tendency to spread to the rectal walls through the lymph channels. Later, lymph thrombosis takes place, and the inflammatory process results in scar formation, with narrowing of the rectal lumen. The entire course of the active phases of the disease may go unnoticed in women as there are no severe subjective symptoms and no visible lesion caused by the primary lesion or the deep-seated lymphatic involvement. Only after a long time, when the late sequelae of the disease appear, is the infection likely to be discovered. This is illustrated

3. Hellerström, Sven: Contribution to Knowledge of Lymphogranuloma Inguinale, Acta dermat.-venereol., 1929, supp. 1, p. 5.

by the case of our patient's mother, whose infection was not recognized even after a colostomy was performed.

Four types of stricture were described by Sénèque:[4] (1) a pure stricture limited to the rectum; (2) a rectal stricture with elephantiasis of the external parts; (3) a rectal stricture complicated by fistulas, and (4) a rectal stricture with pelvic cellulitis. In the case reported here the rectal lesions did not correspond to any of these classifications, which represent late forms of the disease. The rectal lesions found in this patient were acute and early subacute ulcerations which were possibly primary. If such lesions are permitted to spread the end-result may be a progressive inflammatory lesion terminating in stricture. This differs from the strictures seen in most cases, because the drainage in the case reported was direct from the lesion of the mucous membrane in the rectum to the pelvic lymph glands. The manifestations of secondary inflammation were due to a spread from the lesion of the mucous membrane outward into the pelvic glands. In other cases reported the mucosal lesions in the rectum were late and secondary to the involvement of the pelvic lymph nodes. The nodes were affected first by drainage from an initial lesion which was outside the rectum. The rectum at this stage was still uninvolved. The involvement took place only after lymphatic stasis and retrograde infection, the mucous membrane becoming involved last instead of being the seat of the initial lesion. In this case there is no external evidence of another primary lesion. An occult lesion in the vagina or cervix was unlikely, as the hymen was intact and there was no history or evidence of trauma.

ETIOLOGY

Although a variety of organisms have been reported by many investigators, no bacterial etiologic agent has been demonstrated for the disease. Evidence points to a filtrable virus. In 1930, at the Eighth International Dermatologic Congress in Copenhagen, Hellerström and Wassén[5] reported the successful subdural transmission of the disease to apes. One year later Levaditi, Marie and Lépine[6] inoculated human patients with paralysis with a virus that was successfully transmitted through apes several times. Patients infected with lymphogranuloma inguinale seem to be immune to further inoculation. The virus has been reported as being transferable to rabbits, white mice and guinea-pigs.

4. Sénèque, J.: Presse méd. **40**:22 (Jan. 6) 1932.

5. Hellerström, S., and Wassén, E.: Studien ueber die Affinität des Lymphogranuloma inguinal-Virus zu verschiedenen Gewebssystemen beim Affen, Ztschr. f. Immunitätsforsch. u. exper. Therap. **73**:110, 1931.

6. Levaditi, C.; Marie, A., and Lépine, F.: Compt. rend. Soc. de biol. **107**: 1496 (Sept. 18) 1931.

DIAGNOSIS

The most distinctive test for diagnosis is the Frei reaction, which was reported in 1925. The Frei reaction develops after intracutaneous injection of an extract of antigen prepared from the pus of broken-down glands from a patient known to have lymphogranuloma inguinale. The material is diluted to from five to ten times its amount in a sterile solution of sodium chloride and heated in a water bath at 60 C. for two hours one day and for one hour on the succeeding day. Then it is tested for sterility and is ready for use. The antigen is checked on patients known to have lymphogranuloma inguinale; 0.1 cc. is injected intradermally, and the reaction is read in forty-eight hours. A positive reaction is indicated by a red papule at least 0.5 cm. in diameter, having generally a large erythematous halo around it measuring from 5 to 15 mm. in diameter.

The cutaneous reaction is said to develop in a few weeks after the beginning of the initial lesion and to persist for years. It is specific for the disease. Especially in the so-called anorectal syndrome with no visible glandular involvement is the Frei reaction of great value in diagnosis.

In known cases of lymphogranuloma inguinale a positive Frei reaction results, while normal controls or persons with chancroid give a negative reaction. The reaction can be elicited months and even years after the appearance of the initial lesion.

The fact that both parents of our patient had a positive Frei reaction and that the child was born after the disease manifested itself in both parents brings up the question of whether the Frei reaction is transmissible from infected parents to their children. Three children of an infected mother were tested, and all three gave negative reactions. The mother had had the infection for some time when the youngest child (3 years old) was born. Further cases are being investigated in an effort to clarify this question.

Although the disease has been described as venereal, being disseminated mainly through sexual contact, cases have been reported in which the infection has been transmitted in other ways. The infectivity of the lesions may persist for a long time and require the care and precautions employed in other infectious diseases. Perhaps it is wise, in the light of this experience, to warn against an indiscriminate use of rectal tips, common wash cloths and other contacts likely to spread the disease.

TREATMENT

The literature is extensive on the many different types of treatment. This is, perhaps, because of the failure of various therapeutic agents to effect a permanent cure.

Potassium iodide administered internally, emetine intramuscularly and salts of iron, copper, arsenic and mercury have been used. Various types of therapy with foreign proteins, the patient's blood, intramuscular injection of sterile milk and intravenous injection of compound solutions of iodine have been used by various investigators. High voltage roentgen therapy, and therapy with ultraviolet rays and therapeutic heat have been tried with little value. Destéfano and Vaccarezza,[7] Cole [8] and many others reported beneficial results from intravenous injections of solution of antimony and potassium tartrate employed in the form of a 1 per cent solution, the injections being made twice a week in progressive doses, from 5 to 10 cc., in a series of from ten to fifteen doses. Gay-Prieto,[9] Levaditi, Ravaut and Hellerström used intravenous injections of the Frei antigen and claimed some beneficial action. Subcutaneous injections of diluted, sterilized pus from lymphogranulomatous lesions have been used with varying results.

Since the disease is caused by a virus, it is likely that a therapeutic approach along the lines of biologic immunization is the most desirable. The use of the Frei antigen or an attenuated virus has shown some beneficial results. Further investigations in this direction are in progress.

SUMMARY

A case of lymphogranuloma inguinale with rectal lesions in a child of 8 years is reported.

7. Destéfano, F., and Vaccarezza, R. F.: Presse méd. **35**:1378 (Nov. 12) 1927.

8. Cole, H. N.: Lymphogranuloma Inguinale, the Fourth Venereal Disease: Its Relation to Stricture of the Rectum, J. A. M. A. **101**:1069 (Sept. 30) 1933.

9. Gay-Prieto, J.: Dermat. Wchnschr. **95**:1056 (July 16) 1932.

HEMOGLOBINURIA IN CHILDHOOD

FOLLOWING ACUTE TONSILLAR INFECTION

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AND

JOHN O. VAUGHN, M.D.

LOS ANGELES

Hemoglobinuria is rare in childhood. The case reported here is the only one observed in 12,393 infants and children admitted to the medical service of the Los Angeles Children's Hospital from 1920 to 1933. Pediatric literature contains occasional references to this symptom, chiefly as occurring in prenatal syphilis in the form known as paroxysmal hemoglobinuria. Less frequently described is the group of cases in which syphilis is not the etiologic factor. The following case is illustrative of this type.

REPORT OF A CASE

History.—B. B., a white boy, aged 3 years, entered the hospital on Sept. 19, 1933, because of the voiding of red urine. Three days previously he had complained of a sore throat and malaise. Slight fever was noted. The patient's parents attributed the symptoms to an ordinary cold. On the day of admission the child had complained of indefinite abdominal pain and had voided blood-red urine. Both parents and a younger brother were well. The birth and history were not unusual.

Physical Examination.—The boy did not appear to be very ill. He was fairly well nourished, weighing 27 pounds (12,246.9 Gm.). The rectal temperature was 100.4 F. Slight pallor and a suggestive icteric tint in the sclerae were observed. The fauces were inflamed, and a follicular exudate was present on the tonsils; otherwise examination showed nothing abnormal.

Clinical Course.—During the following day, the temperature rose to 101.5 F. and the pallor and icterus rapidly became pronounced. Purpura was not present. The patient hourly became more ill and was considered to be in a precarious condition. Within twenty-four hours he voided only 60 cc. of urine, which was of a black-red, smoky color. The systolic blood pressure was 110; no diastolic reading was obtainable. The hemoglobin, which on admission had been recorded as 62 per cent (Dare), decreased within the first twenty-four hours to 21 per cent. Continuous intravenous infusion was maintained, 5 per cent dextrose in physiologic solution of sodium chloride being employed, and 250 cc. of citrated blood obtained from the child's father was transfused intravenously. Two days after admission to the hospital, the patient's condition was greatly improved, and a similar transfusion was repeated. Improvement was maintained thereafter, and there was a gradual diminution in the degree of icterus and pallor, although the

From the Children's Hospital.

urine remained red until one week after admission to the hospital. On October 9, nineteen days after the onset of illness, the child returned home, apparently normal except for slight general weakness and evidence of chronic tonsillar infection.

Laboratory Data.—Repeated urinalysis during the most critical stage of the child's illness showed blood-colored, semiopaque, scant urine, which often showed a black tinge and which contained a maximum of 800 mg. of albumin per hundred cubic centimeters. The urinary sediment contained a few pus cells, a few granular and hyaline casts and an occasional erythrocyte. The benzidine test gave strongly positive results. The urine contained no arsenic as determined by the Gutzeit method, and spectroscopic examination revealed the characteristic spectrum of hemoglobin, while that for methemoglobin was lacking. Crystals of leucine and tyrosine were not found in the urine, and Millon's test for tyrosine gave negative results. Repeated urinalysis during convalescence reflected the patient's clinical improvement, and ten days after admission the urine was normal. Examination of the blood on entry revealed a hemoglobin of 62 per cent (Dare) and 3,410,000 red cells. The leukocyte count was 15,450. A differential count showed: polymorphonuclears, 77 per cent; small mononuclears, 19 per cent, and large mononuclears, 4 per cent. The stained erythrocytes showed anisocytosis and polychromatophilia. The majority of the polymorphonuclear cells were stab forms, and many showed vacuolation and toxic degeneration. During the second day at the hospital the hemoglobin was recorded as 21 per cent (Dare), and the erythrocytes numbered 1,530,000, with a leukocyte count of 16,100, distributed approximately as on the previous day. Blood platelets were estimated by the method of Fonio as 247,000 per cubic millimeter. Each transfusion produced a marked improvement in the blood picture, and ten days after admission the hemoglobin value had risen to 69 per cent, with 3,480,000 red blood cells.

The Wassermann and Kahn tests of the blood were negative during the acute illness and ten days later. Similar tests were negative in both parents. When the child's hemoglobinuria was most marked, the erythrocytes showed hemolysis beginning with a 0.5 per cent solution of sodium chloride and completed with a 0.4 per cent solution, in contrast to a normal control for whom the respective concentrations were 0.36 and 0.28 per cent. Two days prior to discharge, the resistance of the patient's erythrocytes to hypotonic saline solution was identical with that of a normal control, hemolysis beginning with 0.44 per cent and being complete with a 0.28 per cent solution. When jaundice was most intense, the blood icterus index was 36; at discharge it was 10. The Donath-Landsteiner test gave negative results during the illness and after recovery. When the "chilling test," as employed in cases of paroxysmal hemoglobinuria, was applied to the patient's extremities no hemoglobinuria resulted at six successive hourly intervals. The blood cultures remained sterile. The stools were normal throughout the illness. Roentgen examination of the chest, skull and long bones revealed no abnormalities.

Subsequent Course.—The child remained free from repeated attacks. However, he did not look well; he was undernourished, pale and fretful and had a poor appetite. Examinations of the urine and blood had been repeatedly normal except for slight secondary anemia. The conclusion was drawn that chronic tonsillar infection might be responsible for the delayed recovery. On March 3, 1934, tonsillectomy and adenoidectomy were performed under ether anesthesia. The postoperative course was uneventful. The temperature remained normal except for a brief elevation to 102 F. following surgical intervention. No hemoglobin or blood was noted in the urine after operation. The pathologist reported a definite

increase in the fibrous tissue of both tonsils and marked lymphoid hyperplasia, findings consistent with chronic infection. Culture from the tonsils and adenoid tissue produced Staphylococcus aureus and Streptococcus viridans (alpha type). The Wassermann and Kahn reactions of the blood remained negative. Evaluation of the patient's response to the removal of this focus of infection will be made by future observation.

COMMENT

The relationship of syphilis and paroxysmal hemoglobinuria has been definitely established. MacKenzie [1] stated that paroxysmal hemoglobinuria is usually, and perhaps always, a manifestation of syphilis; syphilis can be demonstrated in more than 90 per cent of the cases by means of the Wassermann reaction. In most instances, clinical evidence of syphilis can be found. In such cases a paroxysm is induced by chilling, however slight, which is followed by the passage of urine colored with hemoglobin. Attacks vary from mild abortive types to severe forms with prostration. Presumably, the serologic mechanism in cases of this sort involves a hemolysin which is absorbed by the erythrocytes in the cold, followed by lysis of the sensitized erythrocytes at higher temperatures if the complement is present. Puris,[2] while admitting that syphilis is the probable underlying factor responsible for the presence of the specific hemolysin in paroxysmal hemoglobinuria, suggested that toxins arising from other infections may be capable of bringing about the same condition. In some cases there may be reasonable doubt as to whether the positive Wassermann reaction signifies a syphilitic infection or a changed condition of the blood serum.

Jones [3] pointed out in his study of pigment metabolism in paroxysmal hemoglobinuria that urobilin is formed in the liver from bilirubin, which in turn is formed from hemoglobin. Following an attack of hemoglobinuria the output of bilirubin is increased in the circulation to approximately three times the normal concentration.

Sellards and Minot,[4] also experimenting with cases of paroxysmal hemoglobinuria, concluded that the liberated hemoglobin is not responsible for the fever, chill and other general symptoms associated with an attack. No toxic symptoms resulted from the intramuscular or intravenous injection of varied amounts of hemoglobin. They further

1. MacKenzie, G. M.: Paroxysmal Hemoglobinuria: A Review, Medicine **8**:159, 1929.

2. Puris, A. M.: Paroxysmal Hemoglobinuria, Am. J. Dis. Child. **37**:1027 (May) 1929.

3. Jones, C. M.: Study of Bile Pigments by Means of the Duodenal Tube in a Case of Hemoglobinuria, M. Clin. North America **5**:1421, 1922.

4. Sellards, A. W., and Minot, G. R.: Injection of Hemoglobin in Man and Its Relation to Blood Destruction with Special Reference to Anemias, J. M. Research **34**:469, 1916.

pointed out that when hemoglobin is injected intravenously, an amount equivalent to at least one sixtieth of that present in the body must be given before it appears in the urine. If, however, hemoglobin is injected into a patient suffering from hemolytic anemia, a much smaller amount is necessary to produce hemoglobinuria.

Hemoglobinuria may be caused by a variety of poisons,[5] such as phenol, betanaphthol, potassium chlorate, oxalic acid, aniline, arsenic, phosphorus, carbon monoxide, chloroform and quinine. Haff disease [6] is a form of hemoglobinuria observed near the Koeningsberger Haff, a bay in the Baltic sea. Arsine, a volatile arsenical base, is deposited in the waters of the bay as a waste product from the adjacent cellulose factories. Ingestion of fish poisoned by arsenic from this source is responsible for hemoglobinuria in fishermen in the vicinity. Hemoglobinuria is also described following severe burns, snake bites or parasitic infections. "March hemoglobinuria" is noted in soldiers as a result of prolonged marching. Similar cases are described as following other varieties of physical exertion.[7] Lordotic hemoglobinuria is reported by Porges and Strisover [8] to be a form of hemoglobinuria induced by walking for ten minutes in a pronounced lordotic position. Constriction of the splenic vessels is suggested as a cause of this variety.

Hemoglobinuria occurs as a complication of the reactions resulting from a blood transfusion when the donor's blood is incompatible. In infancy, Winckel's [9] disease is a rare form of hemoglobinuria, which in the majority of cases is probably due to sepsis.[10] A specific infectious type of the disorder occurs in malarial fever as "blackwater fever." [11] Giffin [12] reviewed the reported cases of hemolytic jaundice with hemoglobinuria. Hemoglobinuria has been reported as a rare occurrence in Raynaud's disease, angioneurotic edema, internal hemorrhage, pernicious anemia and hematuria.[7] Occasional reports indicate that hemo-

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5. Griffith, J. P.; Mitchell, A. G., and Rashford, B. K.: Pediatrics, Philadelphia, W. B. Saunders Company, 1933. Lucas, W. P.: Modern Practice of Pediatrics, New York, The Macmillan Company, 1927.

6. Lockemann, G.: A New Theory Regarding the Etiology of Haff Disease, Med. Welt **6**:1669, 1932.

7. Stephens, J. W. W.: The Hemoglobinurias, Tr. Roy. Soc. Trop. Med. & Hyg. **20**:401 (March) 1927.

8. Porges and Strisover, quoted by Stephens.[7]

9. von Winckel: Deutsche med. Wchnschr. **5**:303, 1879.

10. Anders, H. E., and Stern, G.: Is Winckel's Disease of the New-Born a Sepsis? Arch. f. Kinderh. **71**:101, 1922.

11. Dudgeon, L.: Blackwater Fever, J. Hyg. **19**:208, 1920.

12. Giffin, H. Z.: Hemoglobinuria in Hemolytic Jaundice, Arch. Int. Med. **31**: 573 (April) 1923.

globinuria occurs in a variety of diseases, such as acute respiratory disorders, specific fevers and the exanthems.[13]

In our case a diagnosis of syphilis was excluded by the repeatedly negative Kahn and Wassermann tests of the blood of both the patient and his parents and by the absence of clinical findings of syphilis in the child. In addition, the Donath-Landsteiner test gave negative results, and chilling of the peripheral blood occasioned no hemoglobinuria, which further excluded paroxysmal hemoglobinuria. There was no evidence of contact with chemical poisons or other toxic substances, and we were inclined to regard the definite tonsillitis as the cause of the hemoglobinuria, when the report of McCrae and Ullery [14] appeared. These authors recorded the case of a Sicilian man whose sensitivity to the protein or pollen of the horse-bean (Vicia faba) was manifested by acute febrile hemoglobinuria, prostration, rapidly developing anemia and icterus, with recovery within a few days. They were unable to find similar cases reported in the English or American literature but found occasional reports of the condition in the Italian literature under the term favism.

The patient's parents said that he had not eaten beans in any form for a period of several weeks prior to his illness. However, the child lived one city block from a field of lima beans which was several acres in extent, and although he had not been in the bean field at any time, we felt that the possibility of exposure to wind-blown pollen must be considered. Inquiry revealed that a few plants may have been in bloom at the time of his illness; however, the pollen of the plant is not carried to any extent by the wind. McCrae [15] stated that no information is available in the literature as to the rôle of species of beans other than the horse-bean in the production of hemoglobinuria. No horse-beans were grown in the field in question. Since favism appears to be a form of allergy, Dr. George Piness examined our patient in the allergy clinic of the Children's Hospital. Following an intradermal injection, no reaction was obtained to extracts of the horse-bean and of the skin of the bean.[16]

Our inability to demonstrate allergy toward beans and the presumptive absence of exposure to beans or bean pollen justify the belief that

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13. Wieland, E.: Deutsche med. Wchnschr. **41**:1056, 1915. Kaiser, A. D., and Bradford, W. L.: Hemoglobinuria Occurring in the Prodromal Stage of Chickenpox, Arch. Pediat. **46**:571, 1929.

14. McCrae, T., and Ullery, J. C.: Favism, Report of a Case, J. A. M. A. **101**:1389 (Oct. 28) 1933.

15. McCrae, T.: Personal communication to the authors.

16. Obtained through the courtesy of Dr. Salvatore Parlato of Buffalo.

our case was not one of favism, although the similarity of the clinical course to that described by McCrae and Ullery was remarkable. Accordingly, the conclusion is drawn that hemoglobinuria was precipitated in our patient by an unusual response to acute tonsillar infection. The pathologic physiology of the condition is obscure, and the assumption of such a cause rests largely on the basis of exclusion.

SUMMARY

The occurrence of hemoglobinuria in childhood is reviewed.

An unusual instance is reported of hemoglobinuria in a boy, aged 4 years, which was apparently due to acute tonsillar infection.

1136 West Sixth Street.

TRIPLEGIA FOLLOWING TONSILLECTOMY

EMBOLIC OCCLUSION OF THE ARTERIES OF THE SPINAL CORD

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Embolic occlusion of the arteries of the spinal cord is infrequent and, so far as could be ascertained from a review of the literature, has not been reported as a complication of tonsillectomy. The following case is interesting not only because of the rarity of the lesion but because it was first diagnosed as poliomyelitis.

REPORT OF A CASE

History.—J. K. was sent to the Willard Parker Hospital on Aug. 12, 1929, with the diagnosis of poliomyelitis. The disease was prevalent in the city at that time. The examination on admission revealed an alert and cooperative boy, aged 8 years, with a Fröhlich syndrome. His tonsillar fossae were covered with a grayish membrane and presented the typical appearance after a recent tonsillectomy. There were complete flaccid paralysis and loss of sensation of both lower extremities, the right upper extremity and the muscles of the trunk (fig. 1). The left upper extremity, left half of the chest and entire head were not involved. There was a slight nuchal stiffness. The respiratory rate was not rapid. A slight impairment of speech and inability to cough forcibly were noted. Over the upper part of the chest on the left side was an area of impaired resonance, increased fremitus and bronchovesicular breathing with coarse moist râles. The heart was normal. The temperature was 105 F. on admission. There was incontinence of urine and feces.

The past history was of no special interest. The patient had pertussis and varicella at 3 and measles and a bilateral mastoidectomy at 7 years of age.

Five days before admission (August 7) a tonsillectomy had been performed. The patient remained at the hospital overnight and was discharged the next day. The first afternoon at home he complained of pain in the abdomen and chest; the temperature was 101 F. That night a physician was called and advised the application of a mustard plaster to the chest. The second morning at home (August 10) the patient complained of pain in the right shoulder and vomited after gargling. In the evening he began to cough, and a physician made the diagnosis of pneumonia. The following morning (August 11) his temperature was 105.5 F. The mother noticed that the boy did not move about in bed as much as usual. In the afternoon he was admitted to the Lebanon Hospital, and the following morning he was transferred to the Willard Parker Hospital.

From the Willard Parker Hospital, the Department of Hospitals and the Department of Pediatrics, Cornell University Medical College.

Examination.—The results of laboratory examination of specimens taken at the time of admission were reported as follows: The urine was normal; no Klebs-Löffler bacilli were found in the throat; the red blood cells numbered 4,300,000; the hemoglobin was 80 per cent; the white blood cells numbered 30,600, with 82 per cent polymorphonuclears, 13 per cent lymphocytes and 5 per cent monocytes. The Wassermann reaction of the blood was negative. Blood-tinged fluid was obtained by lumbar puncture. Poliomyelitis was excluded by the history, the distribution of the paralysis and the extensive sensory involvement.

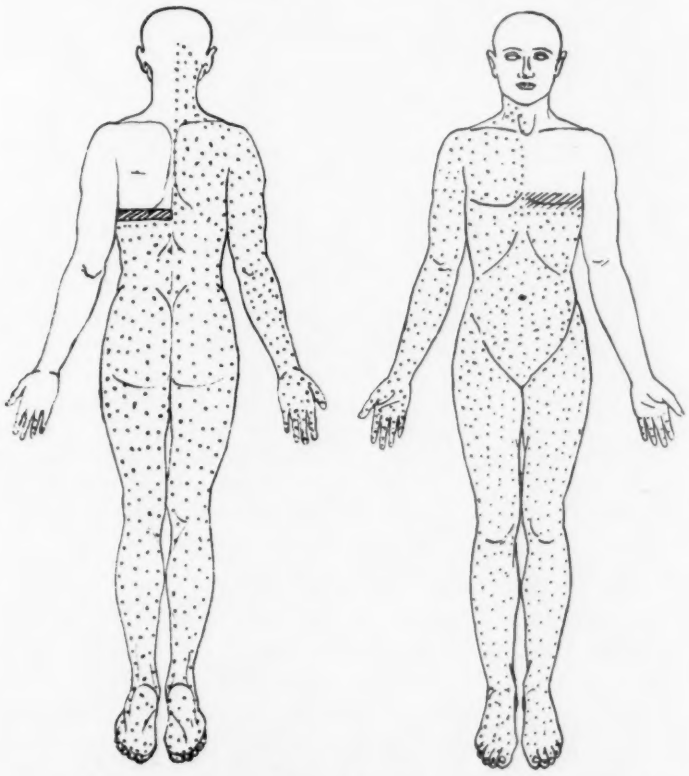

Fig. 1.—Drawing showing condition at the time of admission. The dotted area indicates anesthesia and flaccid paralysis; the shaded area, hyperesthesia. Horner's syndrome was present on the right side.

Course.—The temperature dropped to 102.2 F. on the day after admission. A roentgenogram of the chest showed a small area of consolidation near the base of the right lung. Dr. Thomas Davis saw the patient in neurologic consultation and reported: "There is complete flaccid paralysis of the legs and right arm accompanied by gross and complete sensory loss and complete anesthesia of the right side of the body including the cervical segments and of the left side of the body below the seventh and eighth thoracic segments. At the level of the sixth and seventh thoracic segments there is an area of hyperesthesia on the left side. The abdomen is distended, and there is a dribbling of urine" (fig. 1). The

impression was that of a transverse myelitis, probably infectious. The neurosurgical opinion was as follows: There are complete flaccid paralysis of both lower extremities and the right upper extremity with absence of reflexes and complete loss of pain on the right side to and including the second cervical segment, and on the left side to the midthoracic segments. Horner's syndrome is present on the right side. It is believed that there is also paralysis of the diaphragm. There are marked paralytic ileus and incontinence of urine and feces. The sudden onset of the paralysis with an elevation of temperature shortly

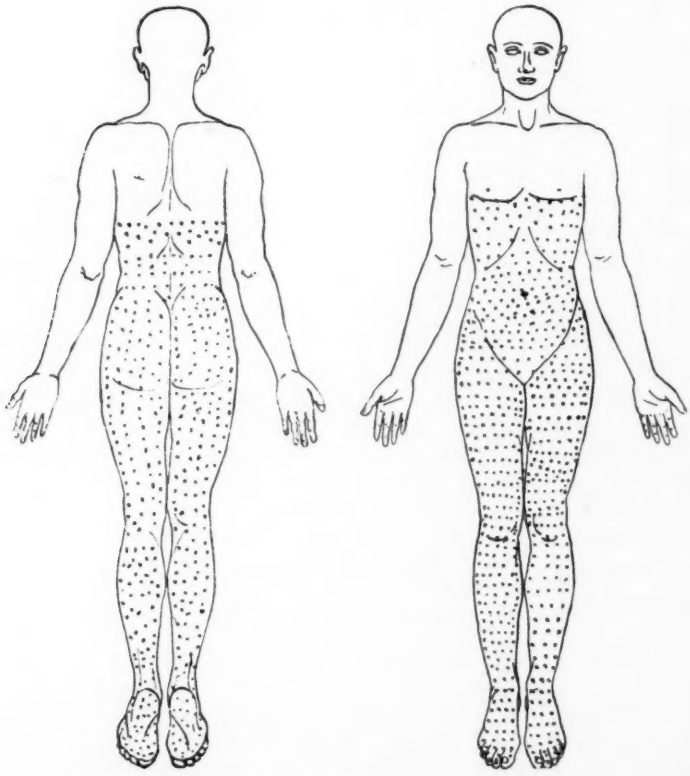

Fig. 2.—Drawing showing the condition after three and one-half years. The dotted area indicates complete anesthesia and flaccid paralysis.

after tonsillectomy suggests an embolic process. Lumbar puncture and manometric test were advised.

The spinal fluid obtained by lumbar puncture on the following day was light yellow and contained 590 cells per cubic millimeter, mostly crenated erythrocytes. There was a slight increase in globulin, and the Wassermann reaction was negative. The manometric readings were normal. Dr. Rosenbluth, chief diagnostician, concurred in the diagnosis of embolic myelitis.

The child's condition remained unchanged for two weeks. After the third day the temperature (except for one elevation) remained under 101 F. for two weeks. On August 26, fourteen days after admission, there was a sudden change.

At 3 o'clock in the morning the nurse thought that the patient was going to have a convulsion. He lost the muscular power in his left arm (previously unaffected) and lost his voice. He rapidly became lethargic and irrational. Several hours later edema of the face, legs and ankles was noted. The urine was blood-tinged. The blood pressure was 100 systolic and 52 diastolic. The following day the temperature rose to 104.2 F. A blood culture made at this time was negative. The patient vomited fluid containing blood. There was bright red blood in the stool. The urine contained blood for several days. After two days the child became brighter and regained the use of the left upper extremity. The edema persisted for several days, then gradually subsided and had disappeared in a week. Following this episode the temperature remained normal except during one period of a few days, the elevation noted at that time probably being due to a combination of cystitis and decubitus ulcer. A month after admission the spinal fluid was normal and the Wassermann reaction negative. The white cell count was 9,800, with 60 per cent polymorphonuclears, 35 per cent lymphocytes and 5 per cent monocytes.

At the time of discharge (Nov. 22, 1929) there were marked improvement in the sensory perception and a slight return of muscular power in the right upper extremity. There was no change in the lower extremities. The urine contained pus cells.

The boy was seen three and a half years after discharge from the Willard Parker Hospital. He was alert and bright. Above the fifth thoracic segment motor power and sensation were normal. Complete function of the upper extremity had returned within a year of the original paralysis. Below the sixth thoracic segment there were complete flaccid paralysis and anesthesia (fig. 2). The deep reflexes were absent and the Babinski reflexes were present on both sides. There was incontinence of urine and feces.

COMMENT

At the time of admission the patient apparently had two embolic lesions, one in the cervical segment and the other in the thoracic segment of the spinal cord. The embolus at the cervical level resulted in a hemimyelitis producing symptoms on one side. The embolic lesion at the midthoracic level produced a complete transverse myelitis. The episode which occurred two weeks after admission was interpreted as a shower of emboli, some of which lodged in the central nervous system, the kidneys, the gastro-intestinal tract and probably other organs. The resulting symptoms subsided after several days.

A year after the original paralysis function of the right upper extremity had returned. After three and a half years there remained a complete flaccid paralysis and anesthesia below the sixth thoracic segment. According to Schaller, Roberts and Stadtherr,[1] acute myelitis is not a progressive disease. It reaches its height within a few hours and thereafter tends toward gradual improvement. In fatal cases death is

1. Schaller, W. F.; Roberts, A. M., and Stadtherr, E. F.: Acute Myelitis, J. A. M. A. **99**:1572 (Nov. 5) 1932.

due to septic urinary infection or to decubitus ulcers. This case bears out these opinions in certain respects. The patient survived after weathering a severe urinary infection and several serious decubitus ulcers. One lesion of the cord gradually and completely healed, whereas the other has remained unchanged, as far as clinical signs are concerned.

A brief consideration of the vascular supply of the spinal cord is of interest.[2] The anterior and posterior spinal arteries arise from the vertebral arteries within the skull. The anterior arteries form a single trunk a short distance from their origin, and this descends along the ventral surface of the cord. The posterior spinal arteries do not unite and descend along the dorsolateral surfaces of the cord. Both arteries are reenforced by segmental spinal branches from the deep cervical, intercostal, lumbar and sacral arteries (branches of the aorta) which

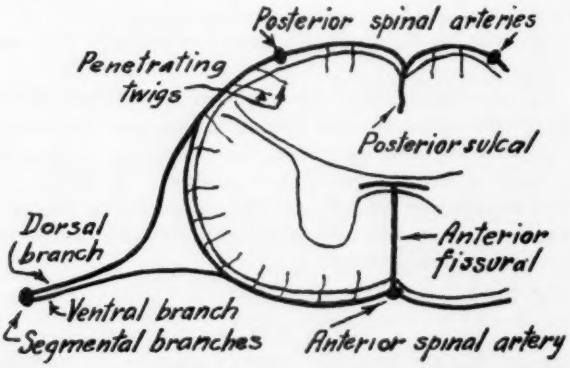

Fig. 3.—Diagram of the main arterial vessels to the spinal cord. Segmental branches arise from deep branches of the cervical, intercostal, lumbar and sacral arteries, which are branches of the aorta.

enter the cord through the intervertebral foramina at various intervals. Branches from these arteries form a series of complete annular anastomoses around the cord and give off penetrating twigs which enter the cord to supply the nerve tissue (fig. 3). The anterior spinal artery gives off the anterior fissural arteries which provide the entire gray matter with the exception of the peripheral zone (Piersol). Branches of the posterior spinal arteries form the posterior sulcal arteries which supply the gray matter of the posterior horns.

With such an extensively anastomosing vascular system it is difficult to determine the location of a lesion that can produce a complete transverse myelitis by cutting off the blood supply. As Winkelman and

2. Piersol, G. A.: Human Anatomy, ed. 7, Philadelphia, J. B. Lippencott Company, 1919.

Eckel [3] stated, that condition cannot result from occlusion of either the anterior or the posterior spinal artery alone. They believe that it may result from an obstruction of the segmental branches from the aorta following aneurysm or formation of sclerotic plaques. According to the same authors [3] previous writers have postulated either a simultaneous occlusion of the spinal arteries or a secondary thrombosis of the posterior supply, as a result of the edema and congestion following occlusion of the anterior artery. It is probable that the lesion in the case reported was due to multiple emboli.

531 East Lincoln Avenue.

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3. Winkelman, N. W., and Eckel, J. L.: Focal Lesions of the Spinal Cord Due to Vascular Disease, J. A. M. A. **99**:1919 (Dec. 3) 1932.

VASCULAR ACCIDENT AND HEMIPLEGIA IN A PATIENT WITH SICKLE CELL ANEMIA

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History.—A colored boy, aged 6, entered Duke Hospital on Aug. 13, 1933, because of headache, dizziness and unconsciousness. He had been well until two days before admission. At that time, he complained of "stomach ache," which disappeared after catharsis. The next morning his head ached and, shortly afterward, he became dizzy and drowsy, and was too weak to climb into bed. His left arm and leg made spasmodic movements and his right limbs were powerless. Speech was only slightly impaired until later in the day, when he became stuporous. He had taken no food or water for twenty-four hours preceding admission to the hospital. The family history was interesting in that a brother had died several months previously after the onset and course of symptoms similar to those of this patient. A sister, aged 12, had had "rheumatism" for several years and her blood smears showed 25 per cent immediate sickling. Smears of blood from the father and mother did not contain any sickle cells. The patient's past history was unimportant.

Physical Examination.—The boy's temperature on admission was 38 C. (100.5 F.); the pulse rate was 120; the respiratory rate was 28, and the blood pressure was 140 systolic and 75 diastolic. The patient was well developed, moderately dehydrated and in a semistuporous state. The skin was dry, and there was general glandular enlargement. The nail beds and mucous membranes were pale, while the sclerae were a deep greenish yellow. The eyegrounds were normal. The tonsils were large, cryptic and moderately injected. The lungs were clear as noted on percussion and auscultation. There was a systolic murmur heard best at the apex and transmitted into the axilla. The right arm and leg were very weak and flaccid. The deep reflexes were hyperactive and the Babinski sign was present on both sides, but remained permanent only on the right side. The cranial nerves were not involved. The spleen was not palpable.

Laboratory Tests.—The blood count showed the following: hemoglobin, 9.8 Gm. (64 per cent) Sahli; red blood cells, 2,740,000; white blood cells, 17,450; polymorphonuclear leukocytes, 80 per cent; large lymphocytes, 8 per cent; small lymphocytes, 8 per cent, myelocytes and transitionals, 4 per cent. There was 25 per cent immediate sickling, and 75 per cent within four hours. Bleeding time was one and one-half minutes and clotting time, one minute. Examinations of the stool and urine and intradermal tuberculin (0.1 mg. with old tuberculin), Wassermann and Schick tests gave negative results.

Course.—Immediately after the patient was admitted to the ward, a lumbar puncture was made and bloody fluid obtained. Clear spinal fluid was collected the next day; however, numerous red blood cells were found microscopically. The

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Pandy, tryptophan and indole tests were negative. The patient remained in a semistuporous condition and the right arm and leg became definitely spastic. Seven days after admission, a cisternal puncture revealed many crenated and sickle red blood cells in the spinal fluid. The patient gradually became less stuporous, and more aware of his surroundings. Later he began to say a few words, and improved steadily. However, three days before discharge (Aug. 29, 1933) right facial weakness developed. The eyegrounds remained normal. He returned to the dispensary at intervals for the next three months and, except for residual spastic paralysis of the right side and right facial weakness, his general condition has been much improved.

COMMENT

One other case in a colored boy, aged 7, has been reported and at autopsy a subarachnoid hemorrhage was found.[1] Cooley[2] and Sydenstricker[3] have seen similar vascular accidents in three patients with sickle cell anemia. Thrombosis of certain vessels, especially those of the spleen, is a common occurrence in sickle cell anemia.[4] Granting that such a tendency is present, might it not follow that occasionally the cerebral vessels are involved? Such an involvement would adequately explain the clinical picture that this patient presents.

NOTE.—Since writing this article, I have observed the case of a colored girl, 4 years of age, who was admitted to the hospital with similar symptoms and signs. The blood picture and the course of the disease were similar to those reported here.

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1. Cook, W. C.: A Case of Sickle Cell Anemia with Associated Subarachnoid Hemorrhage, J. Med. **11**:541 (Dec.) 1930.
2. Cooley: Personal communication.
3. Sydenstricker: Personal communication.
4. Steinberg, B.: Sickle Cell Anemia, Arch. Path. **9**:876 (April) 1930.

Progress in Pediatrics

IDIOPATHIC ANEMIA OF THE NEW-BORN

A REVIEW OF THE LITERATURE AND A REPORT OF TWO CASES

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AND
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In recent years there has come to be recognized a group of cases of severe primary anemia of the new-born. Attention was first drawn to this disease in 1919 by Ecklin,[1] who described a case of severe primary anemia in a 12 day old infant who recovered seven months later. By 1931 Abt [2] was able to collect reports of fifteen cases, which he completely reviewed, and Blackfan and his associates [3] have reviewed a few cases reported since. So far as we are able to determine, thirty-nine cases have been described in the literature. The condition has been designated as "anemia of the new-born" or "congenital anemia." [4] The cases of this type of anemia have been separated from a large group of cases of anemia to conform with Ecklin's original description. The signs and symptoms have been thoroughly reviewed by Abt,[2] Blackfan,[5] Pasachoff and Wilson [6] and others and need not be reiterated here. The purpose of this paper is to report two cases of this interesting condition and to

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1. Ecklin, T.: Ein Fall von Anämie bei einem Neugeborenen, Monatschr. f. Kinderh. **15**:425, 1919. Prior to Ecklin's report Finkelstein (Berl. klin. Wchnschr. **48**:1829, 1911) mentioned a similar case and Lichtenstein (abstracted by Denzer: Arch. Pediat. **43**:738, 1926) admitted the possibility of the occurrence of the condition, but no one described a case until 1919.

2. Abt, A. F.: Anemia of the New-Born, Am. J. Dis. Child. **43**:337 (Feb.) 1932.

3. Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: Erythroblastosis Fetalis and Its Association with Universal Edema of the Fetus, Icterus Gravis Neonatorum and Anemia of the New Born, J. Pediat. **1**:269 (Sept.) 1932.

4. McClelland, J. D.: Congenital Anemia, Am. J. Dis. Child. **35**:732 (April) 1928.

5. Blackfan, K. D.: The Anemias of Childhood, Oxford Monographs on Diagnosis and Treatment, New York, Oxford University Press, 1930, vol. 9, p. 531.

6. Pasachoff, H. D., and Wilson, L.: Congenital Anemia of the New Born: Necropsy and Review of the Literature, Am. J. Dis. Child. **42**:111 (July) 1931.

review briefly the reports in the literature which give particular attention to the blood picture in the cases described. A study of a few of the suggested etiologic factors of this disease has also been made.

ETIOLOGY

The question of etiology is important since a number of possible responsible factors have been named by various observers. The most important etiologic agents that have been suggested are: frequent pregnancies with miscarriages or stillbirths; intracranial or intrasuprarenal hemorrhage; tuberculosis of the mother; asphyxia of the fetus, and the possibility that this type of anemia is a nutritional anemia. The first possibility is ruled out by the lack of a sufficient number of cases of this type, the case of Susstrunk being the only one which seems to substantiate this hypothesis. Were this hypothesis true the abnormal pregnancies would be an effect and not the primary cause. If the anemia is due to any type of hemorrhage it is not to be classified as an example of Ecklin's type of anemia. Tuberculosis of the mother and asphyxia of the fetus were seen in Happ's case,[7] and at the present time and state of knowledge we think it would be better to exclude such cases.

The possibility of a nutritional factor demands more than passing mention. Parsons [8] expressed the belief that congenital anemia is nutritional anemia. In the case which he reported such a condition was simulated, pronounced anemia being present in an infant of 4½ months. To justify this assumption one of two possibilities must be acceptable: (1) that the mother is anemic or potentially so and there is some relationship between her impoverished blood and that of her child; (2) that the blood of the mother is normal but she is unable to impart to the infant the needed iron or perhaps some theoretical blood-forming hormone. In other words, an "impervious placenta" must exist.

The essentials of the first theory may be brought out by two specific questions: Is there any relationship between the hemoglobin content and the number of red cells of the normal mother and that of her infant? Can antepartum therapy administered to the mother affect the offspring? We feel that these questions can easily be answered. In a recent communication, Dr. Phillip P. Barbour [9] stated: "We made the study of some one hundred twenty odd children and we could not

7. Happ, W. M.: Idiopathic Anemia of the New Born Infant, Arch. Pediat. **47**:171 (March) 1930.

8. Parsons, L. G.: Congenital Anemia: A Contribution to the Study of Nutritional Anemia, Acta pædiat. **13**:378, 1932; Deficiency Anemias of Childhood, Lancet **2**:418 (Aug. 19) 1933.

9. Barbour, Phillip F.: Anemia of New Born, South. M. J. **24**:107 (Feb.) 1931.

show that the content of the mother's blood was in any way related to the blood of the new born." This is in accord with the findings of Baar and Stransky [10] and others. The second question is well answered by the experience of Segar and Stoeffler,[11] who reported three cases of anemia of the new-born in offspring from one mother born fourteen and thirty-one months apart. The mother was reported as being in good health, and during the third pregnancy she was given liver extract, beef hemoglobin and a well balanced diet. But in spite of this therapy the third infant began to be anemic at about the same age as the second one. In our first case there was evidence that antepartum treatment of the mother has no influence on the sibling in this type of familial anemia. The mother was given therapy with ultraviolet rays throughout pregnancy along with a carefully supervised diet of a high iron and vitamin content because of the history that her second sibling had died of anemia. Although she was not anemic, and in spite of her treatment, severe primary anemia developed in the third child. With these cases in mind we cannot agree with Parsons that this type of anemia is due to prenatal or postnatal nutritional insufficiency or to actual or potential anemia in the mother.

We realize that these experiences do not disprove the possibility of an "impervious placenta" and of the theoretical hormone; these propositions are at best theoretical.

In table 1 are listed the cases which have been reported in the literature since the appearance of Abt's review.

Of the thirty-nine cases which have been reported thirty-two are undoubtedly cases of Ecklin's type of anemia of the new-born. The remaining nine are excluded because a possible etiologic factor can be found in the history. For example, Greenthal's [12] patient showed intracranial hemorrhage; Foote's [13] patient was a premature twin and the anemia was late in onset like that of prematurity, and in Gregory's [14] case the anemia was undoubtedly due to a streptococcic infectious jaundice. The diagnosis in the remaining six cases is open to question for the

10. Baar and Stransky: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928, pp. 16 and 26.

11. Segar, L. H., and Stoeffler, W.: Anemia in the New Born in Three Successive Siblings, J. Pediat. **1**:485 (Oct.) 1932.

12. Greenthal, R. M.: Anemia of the New Born, Am. J. M. Sc. **179**:66 (Jan.) 1930.

13. Foote, J.: Anemia primitiva en los recién nacidos, Arch. am. de med. **4**:39 (April) 1928.

14. Gregory, H. H. C.: Congenital Anemia with Jaundice, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **2**:92 (Aug.) 1928.

following reasons: Two of the cases (Sanford,[15] Schleussing [16]) may possibly have been instances of erythroblastosis neonatorum. Susstrunk's [17] case was probably one of icterus gravis associated with Ecklin's anemia; also, there were hemorrhages into the pelves of the kidneys. We question the diagnosis in Happ's [7] case because of asphyxia at birth and tuberculous pleuritis of the mother. Pritchard and Smith [18] admitted the presence of hemorrhage into a suprarenal gland in their

TABLE 1.—*Outcome in Cases of Anemia in the New-Born Reported in the Literature Not Previously Tabulated* *

Author	Outcome
1. Sidbury, J. B.: J. A. M. A. **89**: 855 (Sept. 10) 1927	Uneventful recovery
2. Sidbury	Recovery
3. Zahorsky, T. S.: Am. J. Dis. Child. **35**: 165 (Jan.) 1928	Child appeared normal in 10 weeks, but spleen enlarged
4. Nordgren, C.: Hygiea **9**: 981, 1928	Death on fourteenth day
5. Gregory [14]	Not anemia of new-born; streptococci in urine
6. Stransky, E.: Ztschr. f. Kinderh. **51**: 239, 1931	Complete recovery
7. Stransky	Complete recovery
8. Gismondi, A.: Prat. pediat. **8**: 43, 1930	(We were unable to obtain his report)
9. McNeil, C.: Edinburgh M. J. **37**: 175, 1930	Complete recovery at 7 months
10. Lewis. [23]	Complete recovery at 6 months
11. Pritchard [18]	Recovery
12. Bonar, B. E., and Smith, E. H.: Am. J. Dis. Child. **45**: 594 (March) 1933	Recovery at 4 months
13. Dalldorf, G., and Russell, H.D.: New York State J. Med. **32**: 839, 1932	Recovery at 17 weeks
14. Segar and Stoeffler [11]	Recovery at 42 months; patient normal at 4 years
15. Segar and Stoeffler	Complete recovery at 32 months
16. Segar and Stoeffler	Fair recovery at 91 days
17. Bonar and Smith	Complete recovery at 4 months
18. Blackfan [5]	Complete recovery at 7 months
19. Blackfan	Complete recovery at 18 months
20. Blackfan	Complete recovery at 68 days
21. Blackfan	Complete recovery at 63 days
22. Blackfan	Complete recovery at 150 days
23. Blackfan	Complete recovery at 97 days
24. Parsons [8]	Recovery
25. Abbott and Abbott	Complete recovery in 5 months
26. Abbott and Abbott	Death on ninth day

* Since this article was submitted for publication Brown, Morrison and Meyer have reported a case of anemia in the new-born without erythroblastosis in a girl who died on the eighth day of life (Brown, S. S.; Morrison, Maurice, and Meyer, D. A.: Anemia of the New-Born Without Erythroblastosis, Am. J. Dis. Child. **48**: 335 [Aug.] 1934).

Pasachoff and Wilson have recently reported that the mother of their patient has, since this report, given birth to a premature fetus which showed universal edema, thus showing the association of this disease with anemia in the new-born (Pasachoff, H. P., and Wilson, Leo: Association of Universal Edema of the Fetus and Congenital Anemia of the New-Born, Am. J. Dis. Child. **49**: 411 [Feb.] 1935).

case. Parson's [8] case was unlike any other in the literature in that the anemia was late in onset and was not pronounced until the age of 4½

15. Sanford, H. N.: Anemia in a New-Born Infant, Am. J. Dis. Child. **30**:19 (July) 1925.

16. Schleussing, H.: Beitrag zu den sogenannten Anämien der Neugeborenen, Verhandl. d. deutsch. path. Gesellsch. **21**:371, 1926.

17. Susstrunk, G.: Extremely Grave Anemia in New-Born Infant, Ztschr. f. Kinderh. **38**:587 (Aug.) 1924.

18. Pritchard, E., and Smith, J.: Case of Severe Anemia in the New Born Infant, Arch. Dis. Childhood **6**:325 (Dec.) 1931.

months, pointing to an etiology of nutritional insufficiency. We have not included undoubted cases of erythroblastosis neonatorum, such as the case of Frank.[19]

STUDIES OF THE BLOOD

A review of the literature has shown a wide range in the red cell counts and the percentage of hemoglobin, as can be seen in table 2, which contains a summary of the blood counts in forty of the cases now described in the literature. We wish to call particular attention to the high percentage of cases showing a color index of 1 or above. In twenty-two of the twenty-eight cases reported, which is above 80 per cent, the color index was 1 or above. In the majority of the cases the white blood cell count was between 10,000 and 20,000 per cubic millimeter, which is a normal range for infants of this age. The red blood cell counts ranged from 416,000 to 2,800,000 per cubic millimeter. It is sur-

TABLE 2.—*Blood Pictures in All but One of the Cases Reported in the Literature*

Red Blood Cells, Millions	No. of Cases	Hemoglobin, Percentage	No. of Cases	Color Index	No. of Cases	White Blood Cells, Thousands	No. of Cases
2	13 (2,800,000)	40 to 50	10 (48%) (highest %)	1 and above	22	90 to 100	1 (94,000)
						70 to 80	1
1.5 to 2	4	30 to 40	12	Below 1	6	60 to 70	1
						40 to 50	1
1 to 1.5	13	20 to 30	10			30 to 40	1
						20 to 30	8
0.5 to 1	9	10 to 20	6			10 to 20	19
						5 to 10	5
0.4 to 0.5	2 (460,000) (416,000)	0 to 10	1			2 to 5	1 (2,600)

prising that so few infants die in spite of this marked anemia; the immediate transfusions of blood and other therapy are the only reason, no doubt, that more have not succumbed. The differential counts showed no strikingly consistent picture except for the normal or even low monocyte (large mononuclear) count. This will be discussed in more detail later.

REPORT OF CASES

CASE 1.[20]—*Mother.*—The mother was a white American, 30 years of age. She was first seen on Oct. 11, 1932, at which time a physical examination revealed her to be four months pregnant and in good health. She had had three previous pregnancies, two of which came to term with delivery on Oct. 11, 1929, and Jan. 12, 1931. Both infants died in a few days. The third pregnancy was terminated by spontaneous abortion.

19. Frank, E. S.: Congenital Anemia by Erythroblastosis, Nederl. tijdschr. v. geneesk. **2**:1384 (Sept. 25) 1926; cited by Stransky, E.: Beiträge zur klinischen Hämatologie im Säuglingsalter; über die primäre Anämie der Neugeborenen, Ztschr. f. Kinderh. **51**:239, 1931.

20. Dr. C. L. Emmons gave us permission to study and report this case.

Father.—The father was living and was apparently well up to a recent date when he presented a tuberculous spine. The Wassermann reaction of his blood was negative, and he was not anemic.

Sibling 1.—A boy was born on Oct. 11, 1929, after normal labor and delivery with no instrumentation. The skin had a yellowish tinge at birth and became progressively more yellow during the five days of life. On the second day a slight fever developed, and the temperature rose to 103 F. on the day of death. Cough and bleeding from the nose completed the clinical picture on the day of death, October 15. A Wassermann test was not done on either the child or the mother. An autopsy was performed by members of the department of pathology of the Stanford University Medical School, and the report was as follows:

The body weighed 2,590 Gm. and measured 48 cm. The skin was chrome yellow throughout. The umbliical cord was sloughed, the right testicle was undescended and thin blood exuded from the nostrils. The upper and lower lids of the right eye showed small umbilicated tubercles. Examination of the head revealed that the anterior fontanel was open and measured 4 by 3.5 cm. No meningeal or cerebral hemorrhage was found. The thymus was pale yellow and slightly enlarged. The lungs presented the usual picture of hemorrhagic bronchopneumonia. The liver was mottled reddish yellow and measured 1 by 8.3 cm. The cut surface was markedly congested. The surface of the spleen was reddish brown, and the organ measured 5.5 by 3.5 cm. The suprarenal glands and kidneys appeared to be normal. There was no pathologic change in the other viscera.

On histologic examination the lungs revealed the typical changes of hemorrhagic bronchopneumonia. The liver showed a normal capsule, and in the lobules were a number of small fetal blood islands, and quite a few nucleated cells in the capillaries. The spleen, kidneys, suprarenal glands and peribronchial lymph nodes were normal. The diagnosis made on an anatomic basis was: (1) icterus neonatorum and (2) hemorrhagic bronchopneumonia. A subsequent bacteriologic examination of the spleen and bone marrow gave negative results.

Sibling 2.—A boy was born on Jan. 12, 1931, following normal labor and delivery. He gradually became pale and took his food less well. The bleeding and coagulation times were normal. A clinical diagnosis of aplastic anemia was made. There was no fever, and the pulse was good up to the last three or four hours of life. The patient died on January 20 before transfusions of blood could be accomplished.

Autopsy was performed at the San Francisco Children's Hospital by Dr. P. M. Smith. The body was that of a well developed, fairly well nourished male infant 51 cm. long and weighing 2,900 Gm. The skin and mucosa were extremely pale and there was a yellowish tinge to the skin of the face. The head, trunk, extremities and external genitalia were normal. The viscera were all strikingly pale. There was no gross pathologic change in the thoracic cavity. The spleen revealed an unusually firm and dull grayish-red surface with no visible trabeculae or malpighian corpuscles and weighed 32 Gm. The liver weighed 155 Gm. and presented a smooth, pale, brownish-red surface; on section the lobular markings were indistinct. The suprarenal glands appeared normal; the left weighed 6 Gm. and the right, 3 Gm. The pancreas, urinary tract and gastro-intestinal tract were normal. On sectioning the bone the epiphyseal line of the ribs and femur were straight, but the marrow was very pale red.

On histologic examination the capsule of the spleen was seen to be normal, but the malpighian corpuscles were inconspicuous on account of the great cellularity of the pulp. The cells were chiefly large and undifferentiated cells of the primitive myeloid type with numerous eosinophilic myeloid cells. There was a marked scarcity of erythrocytes, and many of the sinuses were empty; some, how-

ever, displayed a few large myeloid cells. The hepatic cells contained heavy deposits of glycogen, and many contained small pigmented granules. Blood islands were numerous but conspicuously poor in nucleated red cells. Heavy infiltrations of eosinophilic leukocytes and myelocytes were seen in the portal spaces. The predominating cells of the bone marrow were undifferentiated types with many eosinophilic myelocytes and an approximately normal number of megalokaryocytes. Erythrocytes were few and chiefly mature. The kidneys, pancreas, suprarenal glands, heart, thymus and other viscera were essentially normal. At that time a diagnosis was made of aplastic anemia with leukemic deposits in the spleen, liver and bone marrow and splenomegaly.

Course of Fourth Pregnancy.—On Oct. 21, 1932, treatment was begun with irradiation of the entire body with the ultraviolet rays from a quartz mercury vapor arc lamp. This was continued every other day until the latter part of December, after which a few days were allowed to intervene between treatments. Therapy was continued until a few days before delivery. The diet was carefully supervised with regard to calories, vitamins and minerals. There was no illness during the pregnancy. Laboratory examination revealed no sugar or albumin in the urine, and the acidity ranged from p_H 5.2 to 7.4. No acetone, diacetic acid or casts were

TABLE 3.—*Hemograms Made During the Fourth Pregnancy of the Mother of the Patient in Case 1*

	Segmented Neutrophils, per Cent	Stab Forms (Band Cells) per Cent	Juvenile Cells, per Cent	Myelocytes, per Cent	Lymphocytes, per Cent	Large Mononuclears (Monocytes) per Cent	Red Cells	White Cells	Hemoglobin (Dare) per Cent	Bleeding Time, Min.
1/20/33	..	..	..	..	..	..	4,860,000	12,000	80	...
2/10/33	..	..	..	..	..	..	4,550,000	11,000	78	...
2/20/33	80	5	0	0	14	1	.....	.....	..	...
3/ 3/33	61	4	0	0	32	1	4,260,000	9,600	..	3

found. There was no hematuria. The Wassermann reaction of the blood on October 14 was negative.

On March 14, 1933, labor was induced, and after four and a half hours of normal labor a male infant was delivered normally.

Sibling of Fourth Pregnancy.—R. W. K., a boy, was born alive at term. He cried lustily, appeared to be well nourished and was of a normal, ruddy appearance. No injuries or malformations of any part of his body were detected. The red blood cell count (table 4) was nearly 2,000,000 below the average normal at birth. The birth weight was 7 pounds and 15 ounces (3,607 Gm.). On the third day he had lost 7 ounces (21 Gm.), after which he gained steadily until on the tenth day he weighed 8 pounds and 2½ ounces (3,678 Gm.). The child's temperature ranged from 98 to 98.2 F. during his ten day stay in the hospital.

On the fifteenth day pallor was noticeable, and this became more marked on the succeeding days. The skin was clear, and not the slightest tinge of jaundice was apparent. The conjunctiva, sclera and mucous membranes were clear. There had been no epistaxis, and no petechial hemorrhages could be found on the skin or mucous membranes. The stools were of a normal color and the urine was not bile-stained nor was bile found on test. Percussion revealed the heart to be of normal size. There were no murmurs, and the rhythm was regular. The pulse was normal. Percussion revealed the liver to be possibly slightly enlarged, and the spleen was palpable. There was slight enlargement of the inguinal and axillary lymph nodes. Following the examination 10 cc. of whole blood was injected into the gluteal muscles.

TABLE 4.—*Analyses of the Blood of the Patient in Case 1*

Age	Red Blood Cells, Millions	White Blood Cells	Hemoglobin,* Percentage	Normoblasts, per 400 White Blood Cells	Macroblasts, per 400 White Blood Cells	Anisocytosis	Poikilocytosis	Bleeding Time	Reticulocytes	Schilling Hemogram: Segmented Neutrophils	Stab Forms	Juvenile Cells	Myelocytes	Lymphocytes	Large Mononuclears	Eosinophils	Basophils	Red Blood Cell Staining	Color Index
1 day.....	4.136	13,600	82 S	Occasional	0	..	..	3 min.	+	42	11	2	2	37	6	0	0	Good	1.0
16 days.....	2.656	10,200	55 S	8	4	+	Slight	..	..	24	11	2	0	11	52	0	0	Light; fair	0.9
18 days.....	2.200	9,800	51 S	1	1	++	Slight	..	0	21	1	2	0	8	68	0	0	Light; fair	1.1
23 days.....	1.664	10,200	36 S	0	0	+++	+	..	0	29	6	2	0	5	55	3	0	Very light	1.1
29 days.....	2.280	11,000	46 S	1	0	+	+	3 min.	+++	34	3	1	0	19	42	1	1	Better	...
35 days.....	2.528	10,800	54 S	1	0	Very slight	Very slight	..	+++	40	2	0	0	26	30	1	1	Better	1.04
44 days.....	2.736	10,600	58 S	0	0	Occasional	Slight	..	..	41	1	0	0	27	30	1	0	Better	...
1 mo. 21 days..	3.062	11,200	68 D	0	0	0	0	..	++	44	1	0	0	29	25	1	0	Begin to be normal	...
2 mo.....	3.320	11,600	74 D	0	0	0	0	..	+	46	1	0	0	30	21	2	0	Better	1.1
2 mo. 3 days...	4.380	9,000	74 D	0	0	Slight	..	..	..	25	1	2	0	61	8	3	0	Very even	...
2 mo. 15 days..	4.790	8,800	78 D	0	0	0	..												
2 mo. 23 days.	4.950	9,000	80 D	0	0	0	0	..	..	26	2	0	0	59	10	3	0	Very even	...
3 mo. 9 days...	4.990	9,600	90 D	0	0	0	0												
6 mo. 12 days..	4.900	8,000	88 D	0	0	0	0	4 min.											
10 mo.....	4.910	12,000	95 D	0	0	0	0	..	..	15	2	0	0	74	8	1	0	Normal	1.0

* The letters S (Sahli) and D (Dare) indicate the method by which the hemoglobin content was estimated.

During the entire course of the anemia we studied the case for a possibility of infectious anemia, but no focus could be demonstrated.

Treatment was commenced on April 3, 1933, with 10 cc. of whole blood given intramuscularly; on the following day 20 cc. was given and on April 10, 15 cc. was given in the same manner (the blood was untyped and was injected into the gluteal muscles). A total of 53 minims (3.23 cc.) of liver extract was administered between April 3 and 16. The hemograms (table 4) show that there was marked primary anemia at this time (sixteenth day of life), which grew progressively worse in spite of the administration of blood and liver extract. On the twenty-third day of life (April 6) iron and ammonium citrate were added to the feeding formula, 10 grains (0.64 Gm.) to each feeding for two days, then 5 grains (0.32 Gm.) at each feeding until May 15. The next blood count showed a decided rise in the number of red blood cells with immature forms present.

When the child was admitted to the hospital on the sixteenth day of life he weighed 7 pounds and 14½ ounces (3,585 Gm.), showing a loss of weight of 2½ ounces (70.75 Gm.) during six days. But during his forty-five days in the hospital he made a steady gain, weighing 12 pounds (5,443 Gm.) when he was discharged.

The patient made an uneventful recovery. He appeared to be normal, had a ruddy color and weighed 21 pounds and 8 ounces (9,755 Gm.) when last seen, on March 20, 1934. The blood picture was normal and showed him to be completely recovered.

CASE 2.[21]—*Mother.*—The mother was a stocky, plethoric French woman of 38. She had had two abdominal operations in 1910 and 1911, respectively. In 1921, at full term, she gave birth to a girl, now 13 years old and well. Another infant, born in 1925, became pale and died on the seventh day of life. In 1926 there was a stillbirth at full term, and six weeks following this a laparotomy was done for the removal of fibroids. During 1927 she received repeated roentgen ray treatments for bleeding uterine fibroids. The treatment reduced their size and produced amenorrhea for two years, after which the menses were reestablished for about one year until this pregnancy. She was admitted to the hospital on Feb. 26, 1932. On Feb. 29 the use of a water-bag followed by manual dilation, was resorted to for dilation of the cervix, and in eight hours a female infant was delivered. Following an abortion of a 3 month fetus with considerable hemorrhage, which necessitated a blood transfusion at the Los Angeles General Hospital, the mother was committed to the Norwalk State Hospital. Aside from the fact that a brother was insane the family history was essentially unimportant.

Laboratory examination revealed a trace of albumin and sugar in the urine. There was no acetone, and the specific gravity was 1.027. The Wassermann reaction of the blood was negative. The hemoglobin content was 67 per cent and there were 3,952,000 red blood cells and 8,000 white blood cells. The color index was 0.87. The erythrocytes stained normally and were regular in size and shape. The differential count was: polymorphonuclear neutrophils, 69 per cent; myelocytes, 1 per cent; small lymphocytes, 25 per cent, and transitionals, 5 per cent.

Patient.—Course: The patient was a fully viable, ruddy girl who cried lustily and appeared to be a full term, normal infant. Her weight at birth was 6 pounds and 10 ounces (3,011 Gm); she lost weight until on the fifth day she weighed 5 pounds and 9 ounces (2,528 Gm.). Following this she gained until the eighth day, when she weighed 5 pounds and 15 ounces (2,699 Gm.)—a loss of 1 pound

21. This was a case of Dr. Albert C. Germann, Los Angeles, who permitted us to report it.

and 1 ounce (483 Gm.) since birth and a gain of 6 ounces (170.4 Gm.) since the fifth day. Supplemental feedings consisted of lactogen. The temperature from the day of birth until the day of death varied from 98.2 to 99 F.

On the fifth day, simultaneous with the increase in weight there appeared scleral jaundice and pallor which increased progressively until the ninth day, the day of death. The pallor was marked and increased rapidly to marble-like whiteness. On the eighth day the baby was given mother's blood and placed in an incubator because of rapid decline, increasing weakness, Cheynes-Stokes' respiration and poor intake of nourishment. There was no response to treatment.

The blood picture on the eighth day was: hemgolobin, 17 per cent; red cells, 744,000, and white cells, 26,000, with 56 per cent polymorphonuclear neutrophils, 0.5 per cent polymorphonuclear eosinophils, 4 per cent myelocytes, 26 per cent small lymphocytes, 10 per cent large mononuclears and 3.5 per cent were unclassified. There was a slight achromasia with a moderate degree of anisocytosis and occasional microcytes, normoblasts and poikilocytosis. There was also a moderate number of macrocytes, and the number of platelets appeared to be normal.

Autopsy: Autopsy was performed by Dr. A. H. Zeiler, of Los Angeles. The body was that of a girl, apparently 10 days of age and weighed slightly in excess of 5 pounds (2,267 Gm.). The membranes were extremely pale. There were no surface abnormalities and no petechiae. The abdomen was not distended, and no abnormalities were found except for pallor. The liver and spleen were normal. There was no increase in fluid in the abdominal cavity. The lungs were well aerated, and there was no free fluid in the pleural spaces. The thymus was not unusually large, and there were no enlarged lymph nodes, either mediastinal or peribronchial. The heart appeared to be normal, and the foramen ovale was closed. There was no evidence of cerebral or meningeal hemorrhage.

Histologic Examination: The microscopic picture of the thymus was not remarkable for a new-born infant. A normal number of Hassall's corpuscles appeared in the sections; they were of normal size and shape. A careful study revealed no unusual foci. The blood vessels appeared to be normal and contained the usual elements except for an occasional nucleated red cell. The thymus was essentially normal. A study of the suprarenal tissue revealed the cells of the cortex and the medulla to be distinct. There were no hemorrhagic areas in either the cortex or the medulla. The medullary portion was vascular, and the blood spaces were filled with red cells, a few of which were definitely nucleated. The suprarenal glands were essentially normal. The lymphoid tissue showed a relative absence of germinal centers. The sinuses were filled with lymphocytes and many nucleated red cells. The capsule was not infiltrated, and there appeared to be a moderate amount of endothelial hyperplasia. The malpighian bodies of the spleen were rather distinct and diffusely scattered and appeared to be fewer than are normally found. The macrophages were abundant, and some of them showed blood pigment. The sinuses were somewhat distended and contained a considerable number of red cells, some of which were nucleated. The cells of the liver were typical and appeared to be normal. The periportal spaces showed heavy infiltration with round cells and nucleated cells with eosin-staining cytoplasm; the latter were undoubtedly nucleated red cells in various stages. The other cells with scant cytoplasm probably were hematopoietic cells. There was a moderate amount of pigment, both phagocytosed and free. This suggested blood pigment rather than biliary pigment. Some of the blood vessels were filled with cells, most of which were nucleated red cells. The bone marrow of the vertebrae and ribs appeared very hyperplastic and very cellular. The exact differentiation of the cells was difficult, but myeloblasts and nucleated red cells were prominent. The bone marrow of the femur was pale and fatty, unlike that of the vertebrae and ribs.

Diagnosis.—The diagnosis was Ecklin's type of anemia of the new-born with marked hyperplasia of the marrow.

COMMENT

Several interesting points concerning this uncommon malady were noted in these two cases. It has been pointed out by others [22] that the condition is familial; this was seen in case 1, which we believe most certainly to be familial, and possibly in case 2. Nine other cases of undoubted familial incidence have already been reported.[23] The amount of hyperplasia that may take place in bone marrow and yet be followed by death is clearly seen in case 2, and this is certainly proof enough of the need of repeated blood transfusions in the severe cases. The two cases here presented represent two clinical types of this disease: In case 1 there was pallor without jaundice, and in case 2 there was pallor with jaundice and the autopsy showed an excess of microscopic amounts of blood pigment in the liver. The significance of the latter observation cannot definitely be settled, but apparently this is another confirmation of Diamond, Blackfan and Baty's [3] belief that the disease is associated with icterus gravis neonatorum, with universal edema of the fetus and possibly with erythroblastosis. Case 1 furnishes an excellent example of the therapeutic value of a combination of whole blood, liver extract and iron (iron and ammonium citrate). We recognize, however, that there are cases in which the condition will respond only to intravenous transfusions of blood.

Another point of interest is seen in our first case, namely, a high count of large mononuclear leukocytes. In no other case of Ecklin's anemia that we know of has this interesting observation been made. The large monocytes were in normal numbers at birth, but the count had increased to 52 per cent on the sixteenth day of life and to 68 per cent on the eighteenth day. These cells increased in number with the increase of the anemia and decreased with the subsidence of the anemia. It is to be noted that greatly increased numbers of mononuclear leukocytes are seen in cases of aplastic anemia, as was reported by Eddie,[24] who found that as high as 52 per cent of the leukocytes were of this type. The only case of Ecklin's anemia reported in which any change in the monocytes was shown was reported on by Abt.[2] Supravital staining of the infant's blood showed a number of large mononuclears engulfing erythrocytes — mononuclear erythrophagocytosis. This has been

22. Diamond, Blackfan and Baty.[3] Segar and Stoeffler.[11]

23. Lewis, Milton Smith, in discussion on Joseph, Hugh Wilson: The Diagnosis and Treatment of the Anemias of Infancy, South. M. J. **23**:1140 (Dec.) 1930. Ecklin.[1] Diamond, Blackfan and Baty.[3] Segar and Stoeffler.[11] Susstrunk.[17]

24. Eddie, E. B.: Primary Aplastic Anemia; Liver Treatment Without Effect, Pennsylvania M. J. **32**:500 (April) 1929.

reported in experimental animals and in association with certain diseases but not with Ecklin's anemia, except in Abt's own case. We regret that we had not seen his article when we began to study our first case, so that we might have looked specifically for this phenomenon.

SUMMARY

The thirty-nine cases of idiopathic anemia of the new-born (Ecklin's type) reported in the literature have been reviewed, and thirty-two of these have been accepted as typical cases. Three cases have been rejected because of an obvious etiologic factor. The remaining six are open to question for various reasons. Special attention has been given to the observations on the blood in this group of cases.

The relationship of this type of anemia to the anemias of nutritional origin was briefly discussed. There seems to be no connection between them.

Two additional cases of Ecklin's anemia are reported. In one the familial tendency is clearly demonstrated while in the other it is not so certain. The familial incidence in nine other cases previously reported is referred to.

Attention is called to the high count of large monocytes in our first case, but no explanation for it has been determined.

Pediatric Biographies

CHARLES MICHEL BILLARD
1800-1832

A NOTE ON THE HISTORY OF HYPERTROPHY OF THE COLON

JOHN RUHRÄH, M.D.
BALTIMORE

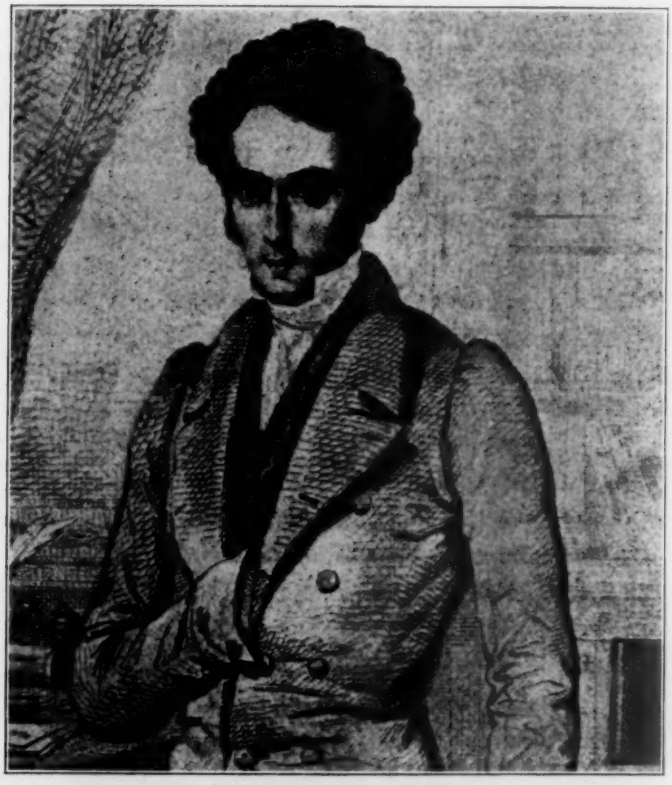
Charles Michel Billard was born on June 16, 1800, at Pellouaille; he studied in Laval and then in Angers, and, deciding on the study of medicine, he went to Paris in 1824 to work in the hospitals. A year later he published his first work, a large treatise entitled: "Recherches d'anatomie pathologique sur les divers aspects sain et morbides que peuvent présenter l'estomac et les intestins." In the same year he translated Thomson's "Principles of Chemistry" and wrote the history of the malformations of the fetus for Chevreuil's book on obstetrics. He obtained a position in the Hospice des enfants trouvés and began his studies on the new-born, which resulted in his "Traité des maladies des enfants nouveau nés et à la mamelle" which was published in 1828, the year in which he was granted his degree. This was followed by the publication of the "Atlas d'anatomie pathologique pour servir à l'histoire des maladies des enfants." Shortly after the publication of this work he returned to Angers, where he died in 1832. In 1833 Ollivier edited a second edition of Billard's work on the new-born. A third edition in French appeared in 1837, and the work was translated into German by Meissner in 1829 and into English by James Stewart in 1839.

Billard was one of the most brilliant of the French physicians interested in the diseases of children, and if he had lived he undoubtedly would have become one of the most noted of all. He was a good clinician and an enthusiastic pathologist, and he pointed out the relation between the clinical symptoms and the pathologic findings. He knew that the infant could have diseases while in utero, and he summed up that knowledge in a remarkable phrase: "Children may be born healthy, sick, convalescent or entirely recovered from a former disease." He made numerous observations on the cerebral congestion of the new-born.

Billard's book, particularly his accounts of his observations on children who died of gastro-intestinal diseases, can be read today with pleasure and profit. The following account of a case of sclerosis of the colon is doubtless an early instance of what is known as Hirschsprung's disease or hypertrophy of the colon. The child showed changes which

were congenital and which corresponded to the first stage of the condition observed by Hirschsprung in 1880 and described by him in 1888. A previous case in an adult had been reported by Parry;[1] subsequent cases were reported by Ebers, Henoch, Peacock, Hughes and others.

The translation of Billard's work was made from the second edition edited by Ollivier.



CHARLES MICHEL BILLARD
1800-1832

FORTY-FOURTH OBSERVATION. CHRONIC COLITIS.
SCLEROSIS OF THE COLON

Joseph Camison, six days old, entered the infirmary September 22. He had a slight icterus, an abundant diarrhea and an advanced state of marasmus. From his birth he had not ceased growing thin. His face profoundly altered expressed continuous pain, numerous furrows marked the brow, the commissure of the lips

1. Parry, C. H.: Collections from the Unpublished Medical Writings of the Late C. H. Parry, London, Underwood, 1825, vol. 2, p. 380.

is drawn outward. He cries but little and nearly always rests immobile in his crib. He died the evening of his entry into the infirmary. On opening the cadaver, there was found a passive congestion of the esophagus, small points of redness in the stomach, the duodenum and jejunem showed only a slight injection, but towards the end of the ileum the walls of the intestines commenced to thicken and became more and more thick as it advanced to the cecum; the opening of the ileo-cecal valve is much retracted and the valve of Bauhin swollen, red and hard. This seat of the thickness is particularly in the submucosa; the mucous membrane is likewise a little thick, very red and friable. The peritoneum is as thin as in normal cases, so that the cellular layer, considerably isolated, forms a single membrane of the thickness of a half line or less, of tissue sufficiently solid and of a whitish aspect like mother of pearl; this tissue, which has nothing more of the cellular, is, on the contrary, of a sort of homogeneity and cuts clearly. This tissue shows the anatomical characters assigned by Laënnec as sclerosis. This state existed in the whole length of the colon.

The intestinal contents were yellowish, liquid and slightly adherent to the intestinal wall.

The liver was blackish, friable and engorged with blood, the bile abundant, viscous and blackish. The lungs and brain were normal.

This lesion of the tissue was without doubt developed during intra-uterine life, and the child had borne with it at birth the chronic colitis of which we shall speak. It is to this disease that the state of feebleness, the diarrhea and the death so soon after birth must be attributed. These two examples of congenital enteritis ought to make clear to us the feeble state in which certain infants are born, whose life has such difficulty in being established inasmuch as they bring with them lesions which through their premature development have altered the germ. This proves again that it is necessary to pay the greatest attention to the causes of feebleness at birth. [The second case referred to was one of a vegetation in the duodenum and some changes in the ileum.]

Pediatrics in Art

DUTCH BABY'S CLOTHING

(SEVENTEENTH CENTURY)

JOHN RUHRÄH, M.D.
BALTIMORE

Franz Hals (1580-1666) of Antwerp and Haarlem painted a Dutch wetnurse and child which now hangs in the Berlin Gemälde Galerie. The nurse has a white cap trimmed with lace and the ruffed collar

Dutch baby's clothing as depicted in a painting by Franz Hals.

of the period. She holds a piece of fruit in her hand, evidently to divert the child, who pays no attention to it but is apparently watching the artist.

The child's dress is a good example of the extreme styles used in babies' clothing, in this case a heavy brocade dress, a cap with fine lace trimmings, a superb heavily starched collar with a lace border and

cuffs and stomacher of the same, the latter being held in place by a jeweled pin.

Clothing of this sort was used in baptismal gowns and for a short period of show might be permitted, but one cannot imagine clothing less suited to early life than these garments, which not only must have been exceedingly uncomfortable but also prevented unrestricted movements and exercise. While it may be poor pediatrics, the picture is an example of Dutch art at its best.

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following were certified by the American Board of Pediatrics since the last report, on Feb. 14, 1935:

E. D. Anderson, Minneapolis; W. W. Anderson, Atlanta, Ga.; H. C. Berger, Kansas City, Mo.; U. J. Busiek, Springfield, Mo.; G. M. Cline, Bloomington, Ill.; W. O. Colburn, Lincoln, Neb.; J. B. Cowherd, Kansas City, Mo.; Vincent Del Duca, Camden, N. J.; D. J. Dolan, New York; David Gingold, Brooklyn, N. Y.; R. E. de la Houssaye, New Orleans; A. W. Jacobsen, Buffalo; C. O. Kohlbry, Duluth, Minn.; P. M. Kurzweil, New York; S. D. Lazarus, Brooklyn; R. H. McBride, Sioux City, Iowa; R. W. McCelvy, Los Angeles; Ellsworth Moody, Joplin, Mo.; C. U. Moore, Portland, Ore.; R. E. Netzley, Pasadena, Calif.; H. C. Niblack, Chicago; J. M. Rector, San Francisco; P. E. Rothman, Los Angeles; H. L. K. Shaw, Albany, N. Y.; D. C. Shelby, Los Angeles; C. H. Smith, New York; O. L. Stringfield, Stamford, Conn.; S. H. Weiner, Boston; E. T. Wyman, Boston.

In this group five applicants were examined. At that examination six were examined; five passed and one failed. In group 1 one failed; in group 2 four passed, and none failed; in group 3 one passed, and none failed.

Physicians Certified by American Board of Pediatrics.—The following applicants have been certified by the American Board of Pediatrics since the last report on March 8:

Louis H. Barenberg, New York; Stanley Brady, New York; F. H. Clark, Jamestown, N. Y.; Harry O. Davidson, Detroit; Clair L. Douglas, Detroit; Ethel Collins Dunham, New Haven, Conn.; William Littell Funkhouser, Atlanta, Ga.; Linton Gerdine, Athens, Ga.; Jesse Robert Gerstley, Chicago; Murray Burnes Gordon, Brooklyn; Benjamin Hoyer, Cincinnati; W. Lloyd Kemp, Detroit; George Clifford King, Fall River, Mass.; James Hall Mason Knox Jr., Baltimore; A. Max Kohn, Detroit; John Allison Nunn, San Antonio, Texas; Harry D. Pasachoff, New York; Donald Wallace Porter, New Haven, Conn.; L. J. Schermerhorn, Grand Rapids, Mich.; Philip H. Sylvester, Boston.

SOCIETY NEWS

American Child Health Association.—The American Child Health Association proposes to have as a special feature of its Child Health Day project for 1935 diphtheria immunization. The object is to bring about cooperation between the departments of health and the medical profession in a campaign for this purpose.

DEATHS

On Dec. 12, 1934, Professor Arthur Keller died at the age of 66. His death was sudden and entirely unexpected.

Keller will probably be best known for his association with Czerny in their book "Nourishment and Disturbances of Nourishment in Children." He was for many years interested in general problems of child welfare and was much respected and looked up to in Germany.

Obituaries

ROGER H. DENNETT, M.D.

1876—1935

Roger H. Dennett was born in Boston on July 21, 1876, and died on Feb. 3, 1935. He graduated from St. Lawrence University with the degree of B.S. in 1898. He received his medical education at Harvard University Medical School, graduating in 1902. After a period of training in the hospitals of Boston he began the practice of medicine in Adamsville, R. I., where he experienced the rigors of a rural practice. In 1906 his name appeared for the first time on the roster of the New York Post-Graduate Medical School as a matriculant in the department of pediatrics where he served as a clinical assistant. In 1907 he became an instructor, in 1913 adjunct professor, in 1920 professor of pediatrics and in 1921 director of the department of pediatrics. St. Lawrence University conferred the degree of Doctor of Science on him in 1928, and at about this time elected him a life member of the board of directors of the university.

He was a member of Alpha Tau Omega, Alpha Mu Pi Omega and Phi Beta Kappa and of the Harvard and University clubs. He belonged to many medical societies, including the Medical Society of the County of New York, the Medical Society of the State of New York, the American Medical Association, the Medical Association of the Greater City of New York, the New York Medico-Surgical Society, the Harvard Medical Society and the New York Academy of Medicine. He was a charter member of the American Academy of Pediatrics. He was consulting physician to the Willard Parker Hospital and the Old Lying-In Hospital, New York; the Victory Memorial Hospital, Brooklyn; the Passaic General Hospital, Passaic, N. J., and the New York Episcopal Orphans' Home and Asylum. At the time of his death he was clinical professor of pediatrics at Columbia University and attending physician in the babies' wards and director of the department of pediatrics at the New York Post-Graduate Medical School and Hospital.

His first book was a guide for mothers which appeared under the title "The Healthy Baby." Undoubtedly his most important contribution to medical literature was "Simplified Infant Feeding," published by J. B. Lippincott in 1915. It is a little difficult at the present time to appreciate the full importance of this work, for what is now commonplace in infant feeding was then considered as revolutionary. The book

was severely criticized by most of the leading pediatricians of the day, but the general practitioner eagerly read it and promptly put its teachings into practice. As the years passed it went into several editions, and unquestionably it had an important part in changing the thought of the medical profession on the problems of infant feeding. Besides these books, numerous articles appeared in both medical and lay journals. Dr. Dennett was considered by some editors as the most able modern-day writer on children's problems for the ordinary reader. It is proper to speculate on the influence of his years as a country doctor on his books and articles, for he seems to have instinctively understood the needs of the average physician and to have known what such a physician could use as he made his rounds among his patients.

As an administrator of a department in the New York Post-Graduate School and Hospital he showed rare qualities of fairness, loyalty and courage and those qualities of mind which go to make personality and character. He was helpful to the younger men of the staff, guarding their interest as he would his own, and he was ready with practical help in time of need. He preached industry, encouraged original thinking and was frankly critical of habits which threatened to defeat what otherwise promised to be a successful career. In all things he was a kindly, interested and enthusiastic friend who gloried in the success of those who interested him. He helped those, if they were deserving, who were personally distasteful to him on the grounds that personalities should not enter into such decisions. He was a good friend and, within the limits of what was honest and fair, a good enemy.

He was intensely interested in his own children and in his grandchildren and in a large measure transferred that interest to all children. Children in turn had an instinctive love for him, for they quickly sense their true friends. It is not to be thought that he would have cared or even have imagined himself practicing any other branch of medicine. To his last day he was doing the things that he liked and loved to do, and his reward lies in that large group of children whose lives he touched and made happier. It is given to few of us to make so great and lasting a contribution to the welfare of children as fell to the lot of Dr. Dennett.

M. C. P.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

AMYLOIDOSIS. H. G. GRAYZEL, M. JACOBI, H. B. WARSHALL, M. BOGIN and H. BOLKER, Arch. Path. **17**:50 (Jan.) 1934.

Amyloidosis was constantly produced in albino mice by subcutaneous or intramuscular injections of a 5 per cent aqueous suspension of sodium caseinate. The amyloid first appeared within the fixed and wandering cells of the reticular system. As these cells disintegrated, extracellular amyloid appeared and increased in amount. It seems probable that amyloidosis is a result of endogenous protein metabolic disturbance rather than a degenerative disease.

Resorption of the amyloid occurred only in mice showing early evidence of amyloidosis. A well balanced, adequate diet caused retardation in the deposit of amyloid. Dry powdered whole liver and vitamins A and B also caused a delay in the production of amyloidosis.

LEMASTER, Evanston, Ill.

THE ANTIGENIC VALUE OF UNPRECIPITATED AND OF ALUM PRECIPITATED TETANUS TOXOID. D. H. BERGEY and S. ETRIS, J. Bact. **27**:95 (Jan.) 1934.

The authors immunized several groups of guinea-pigs with three doses of 1 cc. each of unprecipitated and alum-precipitated tetanus toxoid, using different lots of the former. The antigenic response to immunization with the toxoids was not fully comparable to the toxicity of the original toxins, as measured by the determination of the antitoxic content of the serums and by the amount of standard toxin required to kill the immunized animals. Several groups of guinea-pigs were also immunized with a single dose of alum-precipitated toxoid. The antitoxic content of the serums in these guinea-pigs was apparently higher than that in guinea-pigs receiving three doses of unprecipitated toxoid of the same degree of toxicity of the original toxin, indicating that the immunity response from a single dose of alum-precipitated toxoid was equal to, or greater than, that following three doses of the unprecipitated toxoid. Preliminary experiments were also carried out on man, the results of which will be reported later.

STOESSER, Minneapolis.

A PRELIMINARY NOTE ON A TYPHUS-LIKE VIRUS IN SOUTH AFRICAN RATS. A. PIJPER and H. DAU, South African M. J. **7**:715 (Nov. 11) 1933.

Because Potchefstroom has come to be regarded as the home of a special kind of disease resembling typhus fever, which is similar to, or identical with, Brill's disease, Pijper and Dau performed experiments on animals which showed that Potchefstroom rats harbor a virus similar to that which causes typhus fever and which is different from the virus of tick fever and is closely related to, or identical with, the virus of South African typhus fever. It follows that fleas found on the rats may cause a disease in man similar to typhus fever.

GONCE, Madison, Wis.

THE ACTIVITY OF THE PITUITARY GLAND IN EXCITATION OF THE HYPOTHALAMUS. J. P. KARPLUS and O. PECZENIK, Arch. f. d. ges. Physiol. **232**:402, 1933.

Former experiments of Karplus and Peczenik showed that after stimulation of the hypothalamus in cats the cerebrospinal fluid acted more strongly than before stimulation on the uterus in guinea-pigs and on the melanophores in frogs. This was interpreted as being due to an increased content of the pituitary products

in the cerebrospinal fluid. In the present investigation Zondek and Krohn's "intermedin reaction" of the cerebrospinal fluid (i. e., its effect on the red pigment cells of Phoxinus laevis) was studied before and after stimulation of the hypothalamus. According to Zondek and Krohn, this reaction is caused by a product of the lobus intermedius of the pituitary gland. After stimulation of the hypothalamus in cats the cerebrospinal fluid showed a marked increase of the intermedin reaction. Furthermore, the effect of intravenous injections of the cerebrospinal, fluid on the blood pressure was tested. Stimulation of the hypothalamus increased the pressor effect of the cerebrospinal fluid. The experiments corroborated the assumption that the hypothalamus regulates the secretory activity of the pituitary gland.

SPIEGEL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

A CLINICAL STUDY OF WATER CONTENT OF BLOOD. T. USUI, J. Pediat. (Tokyo), Dec. 20, 1933, p. 2266.

The water content of the blood in normal new-born infants was found to be, minimum, 70.1 per cent and, maximum, 77.7 per cent, with an average of 73.9 per cent. During infancy the average was 82.5 per cent, with a minimum of 80.8 per cent and a maximum of 83.8 per cent. The average during the period of dentition was 82 per cent, and that during early childhood was 80.7 per cent. The average for adults was 81.3 per cent. In infants with nutritional disturbances the water content generally increases. In many infectious diseases there is relatively little change. The water content is also increased in various types of secondary anemia.

KATO, Chicago.

Nutrition

THE VITAMIN A CONTENT OF SKIMMILK, STANDARDIZED MILK, AND CREAM FROM DIFFERENT BREEDS OF COWS. I. L. HATHAWAY and H. P. DAVIS, Agric. Exper. Stat. Univ. Nebraska Research Bull., 1933, no. 69.

Rats depleted of vitamin A were fed skim-milk, standardized milk or cream as the only source of vitamin A. Approximately seven hundred and fifty rats were used in the nine experiments. From these experiments the following conclusions were drawn: 1. The vitamin A content of milk is associated largely with the butter fat, and consequently separated milk containing a small quantity of fat contains only a small amount of vitamin A. 2. The standardization of the butter-fat content of milk by the addition of separated milk reduces its vitamin A potency. 3. In these experiments Holstein cream contained more vitamin A than Jersey cream.

LEMASTER, Evanston, Ill.

THE EFFECT UPON THE GASTRIC JUICE SECRETION OF VARIOUS COOKED PREPARATIONS OF HADDOCK (MELANOGRAMMUS AEGLIFINUS) AND OF LOBSTER (HOMARUS AMERICANUS). A. ALLEY, Am. J. Digest. Dis. & Nutrition **1**:182 (May) 1934.

The interesting experiment in physiology described in this article was carried out on a dog, a pouch from the lesser curvature of the stomach being used. Baked haddock proved the strongest stimulus, followed by smoked haddock, fried haddock, boiled lobster and, last, boiled haddock.

MORRISON, Savannah, Ga.

EFFECT OF DICALCIUM PHOSPHATE WITHOUT VITAMIN D IN THE NUTRITION OF CHICKS. GEORGE M. HIGGINS and CHARLES SHEARD, Anat. Rec. **56**:395, 1933.

Following the report by Bloom that dicalcium phosphate was utilized about 70 per cent more readily than tricalcium phosphate, the authors observed the effect on chicks fed a rachitic diet of adding dicalcium phosphate, tricalcium phosphate and vitamin D in the form of cod liver oil.

The three groups grew similarly for three weeks, then the group given vitamin D gained. The gain in this group was followed by that of the group receiving the tricalcium phosphate, while the dicalcium phosphate group showed the slowest gain. The two latter groups were not as healthy looking, following the weight curve in this respect.

The blood calcium was increasingly lower in the groups which received the tricalcium phosphate and the dicalcium phosphate.

The parathyroid glands of the two groups without vitamin D were markedly enlarged. Degeneration and hyperplasia occurred, and cystlike formations were seen. Likewise, the thyroid glands showed lack of colloid in the follicles, and the epithelium became cuboidal or columnar. Weakness of the legs occurred after the eighth week. There was defective ossification in zones of osteoid tissue. Bone ash determinations were low. Bloom's results, which are the opposite of these, were obtained with rats, and this may explain the discrepancy.

SNELLING, Toronto, Canada.

THE CHEMICAL NATURE OF THE FAT-SOLUBLE VITAMIN OF GROWTH—PHYTOL, CAROTIN, VITAMIN A. M. JAVILLIER, Canad. M. A. J. **30**:473 (May) 1934.

The author reviews the events leading to the development of the present conception of the chemical nature of vitamin A. The chemical formulas of phytol, alpha carotene, beta carotene and the split product of carotene, vitamin A, are discussed.

The conclusions accepted are: 1. Pigmentation due to carotenoid substances present in various materials is not directly proportional to the vitaminic activity of these materials, since not every carotenoid substance acts as an agent of growth. 2. Carotene and the raw material containing it are active, either because carotene has vitaminic activity itself or because it is transformed into an active substance in vivo. 3. The vitamin present in the livers of fish is an alcohol the molecular weight of which corresponds to one half that of the molecule of carotene. It has no color, but there is no longer any reason for expecting that natural substances of vegetable or animal origin should not possess the activity characteristic of vitamin A, even if these substances are not colored with carotenoid derivatives. 4. There is an evident relation of composition and structure existing not only between carotene and vitamin A but also between the active vitamin and the inactive phytol.

MOORE, Omaha.

SOME PHYSICAL AND SOCIAL ASPECTS OF MALNUTRITION IN SCHOOL CHILDREN. JOHN GEORGE SLEVIN, J. Michigan M. Soc. **32**:21 (Jan.) 1933.

Slevin, using the usual criteria for malnutrition, surveyed 1,140 children between the ages of 5 and 14 years attending the Detroit schools. For the purpose of this study, he classified a child from 2 to 15 per cent below standard weight, without clinical criteria, as underweight, and one from 1 to 10 per cent or more underweight, with two or more clinical signs, as malnourished. All others were referred to as the average group. He found that 10.7 per cent of the children were malnourished and 7 per cent underweight. Of the average group, 70 per cent showed demonstrable physical defects, as compared with 89 per cent of the malnourished children and 75 per cent of those underweight. The percentages of defects were definitely greater in the malnourished group.

The conclusions from this study were: (1) Ten per cent of the children in the Detroit schools are malnourished, and 7 per cent are underweight; (2) the malnourished child has more physical defects than the normal child; (3) anemia is the most frequently found defect; (4) anorexia and focal infections are important factors in this problem, and (5) in one third of the children the malnutrition is closely related to the present economic condition.

CAREY, Detroit.

ANTIRACHITIC CONCENTRATES. D. J. BARNES, J. Michigan M. Soc. **32**:242 (April) 1933.

Barnes reviews the recommendations of various authorities regarding the dosage of cod liver oil. Because of the probable intolerance of doses of oil sufficient to act as a curative agent in rachitis, he recommends a concentrate. He also stresses the importance of including adequate doses of vitamin A along with the vitamin D. He states that viosterol is not equal, unit for unit, with cod liver oil in preventing and curing rickets, nor does irradiated ergosterol possess the same vitamin D as is represented in cod liver oil.

Halibut liver oil, known as haliver oil, contains one hundred times the vitamin A content and from fifteen to twenty times the vitamin D content of plain cod liver oil. The dosage is difficult to regulate, as 2 minims of this oil furnishes as much vitamin A as 3 teaspoonfuls of cod liver oil, and the same amount would furnish only as much vitamin D as is represented by from 30 to 40 minims of cod liver oil. Barnes relates briefly his experience with vitamin D milk in a special experiment which was being carried on at the time of writing.

CAREY, Detroit.

VITAMIN D MILK—A RÉSUMÉ. SAMUEL FRIEDMAN, J. Pediat. **4**:678 (May) 1934.

The subject of vitamin D milk is considered under the following headings: (1) direct irradiation of the milk, (2) feeding of vitamin D concentrates to cows, (3) irradiation of cows and (4) direct addition of vitamin D concentrates to the milk.

The history of the development of vitamin D milk is considered in detail, and some of the present unsolved problems in this field are discussed.

LEMASTER, Evanston, Ill.

VITAMIN A CONTENT OF FOODS AND FEEDS. G. S. FRAPS and RAY TREICHLER, Texas Agric. Exper. Stat. Bull. 477, July 1933.

The units of vitamin A activity were estimated (in rat units) in over 107 samples of foods and feeds. They are tabulated with other estimations of vitamin A in the literature. The quantity of vitamin A decreased during storage of alfalfa, dried whole milk and other foods. The process of drying foods caused a loss in vitamin A. There was a fairly constant gain of vitamin A during the period of growth of yellow corn. As previously shown, the vitamin A content of butter and eggs depended on the food eaten by the animal. Human beings are provisionally estimated to require 1,000 units of vitamin A a day. The following foods offer this quantity of vitamin A for one-half cent a day or less: bananas, carrots, yellow corn, cod liver oil, collard greens, liver, mustard greens, spinach, sweet potatoes and turnip greens. Other sources of vitamin A are discussed, and a table gives the relative cost of vitamin A in a number of feeds at the specified prices.

LEMASTER, Evanston, Ill.

THE DIET OF TEXAS SCHOOL CHILDREN. JESSIE WHITACRE, Texas Agric. Exper. Stat. Bull. 489, 1934.

This report is based on a survey of the diet of Texas school children, with special regard to regional, seasonal and racial differences. The subjects included 993 white children, 471 Negro children and 153 Mexican children from different parts of the state. Racial differences in regard to the kinds of foods used were less marked than is commonly supposed. All three racial groups appeared to have a deficiency in the use of milk, fruit, vegetables and whole cereals. The Mexicans drank a great deal more tea and coffee than either the white or the Negro children. Girls had slightly better diets than boys. There was little difference in the diets at various seasons of the year and in different districts. The findings suggest that there are good reasons for continued emphasis on the liberal use of milk, fruits, vegetables and whole cereals in the diet of growing children.

LEMASTER, Evanston, Ill.

RENAL LESIONS IN HYPERVITAMINOSIS D. J. GOUGH, J. B. DUGUID and D. R. DAVIES, Brit. J. Exper. Path. **14**:137, 1933.

The occurrence of calcification and parenchymatous degeneration ("nephrosis") in the rat's kidney in hypervitaminosis D was investigated. The two lesions, which frequently coexist, were found to be largely independent of one another. Calcification went parallel with a high renal excretion of calcium. Nephrosis could not be clearly correlated with any of the urinary disturbances recorded, but seemed to be in a large measure dependent on the administration of sodium biphosphate, U. S. P., with overdoses of vitamin D. The effects of large doses of the acid and alkaline orthophosphates, both with and without hypervitaminosis D (20,000 M.R.C. units of vitamin D substance daily), were compared. The urinary excretion of calcium and the deposition of calcium in the kidneys were found to be greatest when the alkaline phosphate was given, and especially when the vitamin D substance was added. The urinary excretion of phosphorus was greatest when the acid phosphate was given. The vitamin D substance had the effect of lowering it, both when the acid and when the alkaline salt was given. The amount of phosphorus found post mortem in the kidney was greatest when the vitamin D substance had been given with the acid diet, and it was in these circumstances that the most severe nephrosis developed. The large accumulation of phosphorus in the kidney in the nephrotic rats was thought to be a mark of retention of phosphates caused by the renal disease. The urinary excretions of calcium and phosphorus appeared to show a reciprocal relationship to one another, a relative elevation of the one being accompanied by a corresponding lowering of the other.

AUTHORS' SUMMARY. [ARCH. PATH.]

FOOD AND GOITRE. ROBERT MCCARRISON, Brit. M. J. **2**:671 (Oct. 14) 1933.

The size of the thyroid gland within normal variations is discussed. There are two important considerations in the study of the activity of the thyroid gland or its diseases. These are: the influence of the gland on the metabolism of food and the influence of food on the gland.

The physiology of the thyroid gland is discussed, with special reference to its influence on the metabolism of various foods. This is discussed from the standpoint of animal experimentation as well as from what is known of human physiology. Then follows a discussion of the influence of food on the thyroid gland. There are two main directions in which food may influence the gland: It may impose on the organ a burden of work greater than it can bear without undergoing hypertrophy and subsequent fibrosis due to strain, or, because of improper food, the physiologic efficiency of the gland may become impaired. Under perfect conditions, when the constitution of the diet is normal, there is less variability in the size of the thyroid gland. Experiments on that phase are outlined. From these experiments it is shown that: (*a*) the size of the thyroid gland is profoundly influenced by the composition and quality of the diet; (*b*) true goiter can arise despite the adequate ingestion of iodine as potassium iodide, and (*c*) vitamin insufficiency has an important relation to goiter.

Oxygen deficiency and the formation or development of goiter are then discussed briefly, likewise vitamin deficiency and goiter, with particular reference to the deficiency of vitamin C in a patient on a scorbutic diet, which the author thinks not infrequently conduces strongly to the formation of goiter.

Iodine deficiency in the development of goiter is then discussed along well known lines. The author believes that iodine deficiency alone is not the cause in all instances, if in any, in the development of goiter, but thinks that there is an intimate action between iodine, the thyroid gland and a general or so-called balanced ration.

ROYSTER, University, Va.

LACTATION ASSOCIATED WITH BLEEDING FROM THE BREASTS. A. M. CLAYE, Brit. M. J. **1**:665 (April 14) 1934.

A case of bleeding from the breast along with lactation is reported in a primipara, aged 29. The blood was mixed with milk in large proportion; the bleeding subsided spontaneously within a few weeks. The author refers to several other cases of this type reported by various authors and quotes Fitzwilliams, who thinks that the condition is due to "apparently simple engorgement prior to the establishment of milk." In all the cases reported the condition cleared up without any subsequent complication.

ROYSTER, University, Va.

DIET AND THE TEETH: PART III. THE EFFECT OF DIET ON DENTAL STRUCTURE AND DISEASE IN MAN. MAY MELLANBY, Medical Research Council, Spec. Rep. Ser. no. 191, 1934.

This is the third of the reports written by Mrs. Mellanby for the Medical Research Council on the teeth, giving an account of her investigations since 1917. In the work reported experiments on animals were extended to children, to determine whether dental disease in man is mainly a problem of nutrition and, if so, how it can be prevented.

As a result of these long-continued investigations, Mrs. Mellanby states that perfectly calcified and regularly arranged teeth can be produced by including in the maternal diet during pregnancy and lactation and in the diet of the offspring at the time of dental development substances containing an abundance of fat-soluble vitamins, calcium and phosphorus, such as milk, egg yolk, fish and animal fats. Vitamin D can also be obtained by exposing the skin to sunlight. Cereals, especially those rich in embryo, such as oatmeal, tend to produce badly developed (hypoplastic) teeth and call for a correspondingly larger supply of calcifying foods for good development. The majority of children in the British Isles have teeth of imperfect structure and rough surface, which are much more likely to be attacked by dental caries than are perfect teeth with smooth surfaces. The resistance of teeth to caries can be increased independently of their original structure by giving a diet of high calcifying activity. Resistance can be decreased by a diet rich in cereals and of low calcfying properties.

The experimental work indicated that a deficiency of vitamin A or carotene plays an important part in the development of periodontal tissues and in the control of the onset of periodontal disease, including pyorrhea.

In order to substantially reduce the incidence of dental disease in the temperate zones drastic changes in diet are necessary. The consumption of milk, eggs, cheese, animal and fish fats and vegetables must be greatly increased and the intake of cereals correspondingly diminished. The author advises that no cereal be given the very young infant and urges that breast feeding be prolonged up to a year or more, provided that after 6 months of age a supplementary diet including iron, vitamin C and the fat-soluble vitamins is given.

LEMASTER, Evanston, Ill.

THE CHEMISTRY OF MILK. M. L. BABONNEIX, Gaz. d. hôp. **107**:275 (Feb. 24) and 306 (March 3) 1934.

The author gives a general review of the subject, which is rather elementarily treated.

KAJDI, Baltimore.

FISSURES OF THE BREAST. H. VIGNES, Nourrisson **22**:18 (Jan.) 1934.

Attempts made during pregnancy to render the breast more resistant to the development of fissures have not met with success. After the baby begins to nurse he should not be allowed to prolong unduly the nursing periods. After fissures have developed, local applications containing bismuth, silver nitrate or balsam of Peru are recommended. During the acute stages it may be necessary to use a nipple shield or, still better, to draw out the milk with an electric breast pump.

MCCLELLAND, Cleveland.

INSULIN AND THE HYPOTROPHIC INFANT. G. SANPAOLESI, Riv. di clin. pediat. **32**:3 (Jan.) 1934.

The author studied the effects of injections of insulin in five undernourished infants. He did not observe any favorable effects on growth in the doses used (2 or 3 units daily). Insulin diminished the number of stools daily, which rendered possible the ingestion of a higher percentage of carbohydrate in the food.

The author is of the opinion that it is dangerous to give insulin in larger doses than he used.

HIGGINS, Boston.

FUNCTION OF BILE IN THE DIGESTION OF FAT; REPORT OF THREE CASES OF MALFORMATION—CONGENITAL ATRESIA—OF THE BILE DUCTS. D. MOGGI, Riv. di clin. pediat. **32**:257 (March) 1934.

The author reports three cases of congenital atresia of the bile ducts in children. He reports data obtained on studies of the fat balance of these children and of a normal child; all the children received mother's milk.

The results are given in the following table:

	Case 1	Case 2	Case 3	Normal Baby
Percentage of ingested fat excreted in feces..	55.6	33.3	27.8	3.9
Percentage of fecal fat excreted in feces				
As neutral fat.....	17.8	24.9	25.9	10.0
As fatty acids.....	46.8	64.5	68.5	54.4
As soaps	35.4	11.2	5.6	35.7

The author concludes that in congenital atresia of the bile ducts the elimination of fat by the stools is greatly increased. However, the excretion of neutral fat is not much increased over that of the normal child, indicating that bile is unnecessary for the hydrolysis of fat. The percentage of soap in the stools is variable, the amount being somewhat dependent on the individual acid-base equilibrium.

HIGGINS, Boston.

ACTION OF ULTRAVIOLET RAYS ON HEXOSE DIPHOSPHORIC ACID ADDED TO THE BLOOD SERUM OF NORMAL AND RACHITIC CHILDREN. G. FRONTALI and A. ROSSI, Riv. di clin. pediat. **32**:276 (March) 1934.

Hexose diphosphoric acid and inorganic phosphoric acid undergo a reversible reaction in the blood serum. The former does not react to the usual tests for inorganic phosphorus and is classed as organic phosphorus.

The authors describe in vitro experiments made on the blood serums of normal and rachitic children.

Ultraviolet irradiation of these serums increased the inorganic phosphorus, producing a shift of organic to inorganic phosphorus.

When hexose diphosphoric acid was added to the serums an increase in the inorganic phosphorus was found, something in the serums being responsible for changing some of the hexose diphosphoric acid to inorganic phosphate.

Irradiation of the serums to which the hexose diphosphoric acid had been added was then carried out. In the serums of 75 per cent of the normal children the inorganic phosphorus was increased. In ten of eleven serums of rachitic children irradiation resulted in a diminution of the inorganic phosphorus.

The interpretation of these findings seems to lie in the recognition of physicochemical differences in the serums of rachitic and normal children, especially as regards the reversible reaction between organic and inorganic phosphorus.

HIGGINS, Boston.

INVESTIGATIONS ON THE FORMATION OF COLOSTRUM. MARTIN HOHLFELD, Jahrb. f. Kinderh. **138**:185 (Feb.) 1933.

Observations on several lactating goats showed that if they were not milked the secretion of the mammary glands gradually took on the characteristics of

colostrum. One goat became pregnant during lactation; the goat was milked each day, including that on which the kids were born; at this time, she had normal milk and not colostrum.

CLAUSEN, Rochester, N. Y.

CONCENTRATED BARLEY GRUEL. M. J. OLEWSKY, S. A. GILL and S. B. RODKIN, Jahrb. f. Kinderh. **138**:219 (Feb.) 1933.

Introduced as a substitute for gruel made of rice, which is expensive in Russia because it must be imported, 10 per cent barley gruel was found to be useful in the treatment of various acute nutritional disturbances in 131 infants.

CLAUSEN, Rochester, N. Y.

THE MINERAL CONTENT OF THE BLOOD DURING THE FIRST YEAR OF LIFE. J. A. KOTIKOFF, Jahrb. f. Kinderh. **138**:280 (March) 1933.

Repeated observations were made on twenty-one infants during the first year of life to determine the content of serum potassium and sodium by the method of Kramer and Tisdall, of organic and inorganic phosphorus by the method of Samson and of calcium by the method of de Waard, through all the months excepting July and August. Citations from the literature are made, and numerous tables are presented, giving the average values and the range of values. The average value for calcium at the age of 2 weeks was 13.7 mg. per hundred cubic centimeters (eight cases), and at 1 month, 11.8 mg. (thirteen cases). The author fails to state the number of determinations in most cases and to give standard deviations or probable errors. It is therefore impossible to know whether the variations in the mean values in the tables are significant. The ratio of calcium to phosphorus is calculated as that of mean calcium to mean phosphorus, instead of that of the mean to the calcium-phosphorus quotient, and other ratios of minerals likewise, and therefore they lose much significance.

CLAUSEN, Rochester, N. Y.

CHEMICAL CONTRACEPTIVES AS A CAUSE OF RETARDED GROWTH. FELIX SCHLIESSNER, Kinderärztl. Praxis **4**:4 (Jan.) 1933.

Schliessner's theory is that chemical contraceptives may cause serious damage to spermatozoa without interfering with their motility. It is possible for such a spermatozoon to fertilize an ovum, but the child resulting from such a union may be physically below par. He reports three cases of hypoplasia which might be explained on this basis. He requests more observations by other physicians.

HUENEKENS, Minneapolis.

THE TREATMENT OF PERIODIC VOMITING WITH ACETONEMIA IN CHILDHOOD. RICHARD UNGAR, Kinderärztl. Praxis **4**:11 (Jan.) 1933.

Ungar believes periodic vomiting to be a sign of acute intoxication due to a disturbance of nervous regulation of the carbohydrate metabolism. He gives by mouth small and increasing doses of Carlsbad mineral water to which is added 5 per cent grape sugar. After the acute symptoms have subsided, the child is placed on a diet rich in carbohydrate and low in fat for three or four weeks.

HUENEKENS, Minneapolis.

PROPHYLAXIS AND THERAPY OF AVITAMINOSIS IN CHILDHOOD. RICHARD WAGNER, Wien. klin. Wchnschr. **46**:241 (Feb. 24) 1933.

Wagner writes that in normal times the danger of avitaminoses is remote if the diet is kept as varied as possible, with the inclusion of sufficient fresh foods. Adults with healthy nutritive instinct suffer only infrequently from avitaminosis in the temperate zones. There is, however, a difference in infants; special dangers

exist for the artificially nourished infant, as well as for the older child who is dependent on adults with regard to foods. Diet is not only faulty in the absence of important vitamins, but also is insufficient when less than the minimal amount of these substances is present over a period of time. It is possible that increased susceptibility in winter, when respiratory infections are numerous, may be due to a vitamin deficiency. When a great number of children are to be nourished, as in institutions, the vitamin content of foods must receive the greatest consideration in the planning of the diet.

Two avitaminoses especially to be avoided in infants are xerophthalmia and infantile scurvy. Xerophthalmia comes into existence through the absence of fat-soluble vitamin A. This is present in both human milk and cow's milk. Since it is heat-resisting, there is no objection to boiling the milk. Lengthy pasteurization does not destroy vitamin A. Skimming and dilution of milk, however, decreases the vitamin A content considerably. The largest part of vitamin A in milk is in the fat. During prolonged use of buttermilk or skimmed milk in the feeding of infants it should not be forgotten to add vitamin A in some other form. Premature infants, twins and debilitated infants, as well as children suffering from icterus, are especially subject to xerophthalmia. In older children xerophthalmia is generally preceded by hemeralopia. Xerophthalmic infants, like other children suffering from avitaminoses, are prone to infections, so that the final cause of death is given as infection. After therapy is introduced, the lack of growth may be made up in children in the first year of life, but not in older children, who remain small in spite of the most energetic treatment. It is therefore clear that the most important measures in xerophthalmia are prompt early diagnosis and prophylaxis. The only remedy to be considered is cod liver oil, since it contains vitamin A in the greatest concentration. Spinach, tomatoes, carrots and milk contain vitamin A, but they will scarcely serve as remedies, particularly as the vitamin A content of milk fluctuates greatly, depending largely on the time of year and the fodder of the cows.

ABT, Chicago.

STANDARDS OF SIZE AND WEIGHT IN CHILDREN AND JUVENILES. WERNER KORNFELD, Wien. klin. Wchnschr. **46**:683 (June 2) 1933.

Kornfeld states that in spite of the continued poor economic conditions, the average bodily size of German and Austrian children, which had decreased markedly during wartime, has not only equaled, but seems to have exceeded, the prewar average. These changes are the continuance of a tendency noted before the war, which, in view of the increased growth of children of the broadest strata of population, virtually results in a lesser advance in weight.

This increased growth and slenderization of children, in spite of the miserable economic conditions, are largely ascribed to a healthier mode of living, particularly in respect to bodily action, sport and fresh air.

ABT, Chicago.

THE RÔLE OF STRONGLY UNSATURATED FATTY ACIDS IN METABOLISM. HARALD TANGL and MIKLOS BEREND, Magyar orvosi arch. **34**:133, 1933.

Unsaturated fatty acids with four double bonds play an important rôle in fat metabolism. During the digestion of fat a part of the fat becomes strongly unsaturated because of the effect of the pancreatic juice and bile. The unsaturated fatty acids produced this way are water-soluble at body temperature and dialyzable. This desaturation may be due to enzyme action. There is no change in the amount of the unsaturated fatty acids with four double bonds during starvation. From 5 to 10 per cent of the fat content of the blood is composed of these fatty acids, and they are found in greatest amounts in the liver. During the absorption of fat the fatty acids of the blood with four double bonds increase, following an initial decrease. There is no initial decrease, however, if besides fats carbohydrates are absorbed.

KUGELMASS, New York.

RAW TOMATOES FOR DIARRHEA IN CHILDREN. F. GRODECKI, Pedjatria polska **13**:35, 1933.

Grodecki states that he has used raw tomatoes for diarrhea for thirty-five years, with great success. He uses fresh, ripe tomatoes grated or in the form of juice, which he frequently gives in doses of 1 teaspoonful or more. He attributes the action of the tomatoes to their acids and their abundance of vitamins.

KRUPINSKI, Chicago.

INFLUENCE OF THE PROPHYLAXIS OF RICKETS ON THE MILK TEETH. J. J. SOER, Maandschr. v. kindergeneesk. **3**:280 (April) 1934.

For three years the author prescribed for 536 children at his infant welfare center in Dordrecht a preparation of vitamin D, to prevent rickets. The results were controlled by roentgenograms of the wrist. Of the treated children only 6 showed mild rickets. Later, the author studied (following the example of Mrs. Mellanby) the deciduous teeth of 180 children, now about 8 years old, to determine the influence of previous rickets. Any sign of rickets which the children had presented in their first year and the amount of vitamin D which they had received were known from the first experiment. Even among the children who received sufficient antirachitic prophylaxis a high percentage of carious teeth was observed. The author concludes that, as the crowns of the deciduous teeth are already finished at birth, it should be necessary to treat the mothers during pregnancy to prevent caries in the deciduous teeth of the children. The prophylactic treatment of rickets should have more effect on the permanent teeth.

VAN CREVELD, Amsterdam, The Netherlands.

METABOLISM OF MINERALS IN THE ANIMAL ORGANISM: III. MANGANESE. E. SLUITER, Nederl. tijdschr. v. geneesk. **77**:1553 (April 8) 1933.

In this review the occurrence of manganese in living organisms, its resorption, fixation and excretion in the animal body, the symptoms caused by its resorption and its biologic activity are discussed in detail. Manganese is widely distributed in plants and animals. It enters the animal organism principally by way of the digestive tract. The greater part is excreted in the feces, not in the urine. Under different conditions its resorption may give rise to intoxication. From its constant presence, it may be concluded that manganese is a substance of importance to the organism. However, the functions of manganese and the specificity of those functions have not as yet been established. The difficulties of determining the biologic action of minerals—which, for the greater part, are substances with an oligodynamic action—are principally due to the fact that it is nearly impossible to work with products which are free from the substances to be examined.

VAN CREVELD, Amsterdam, The Netherlands.

LIPOID PHOSPHORUS AND INORGANIC PHOSPHORUS CONTENT OF THE BLOOD AND ULTRAVIOLET IRRADIATION. H. STIEMENS and G. C. HERINGA, Nederl. tijdschr. v. geneesk. **77**:1635 (April 15) 1933.

One of the authors found that ultraviolet irradiation under certain conditions caused a remarkable change in the distribution of the lipoids in the epidermis and gave rise to the presence of cells loaded with lipoids round the blood vessels of the stratum papillare. The authors then undertook an investigation to determine whether the lipoid phosphorus content and the amount of inorganic phosphorus in the blood were modified by such irradiation. They found that irradiation of the skin of a great number of healthy students had no effect on the lipoid-phosphorus content of the blood. The amount of inorganic phosphorus was increased by the irradiation.

VAN CREVELD, Amsterdam, The Netherlands.

Relation Between the Nature of the Food and the Degree of Rickets in Rats. M. de Bruin, Nederl. tijdschr. v. geneesk. **78**:397 (Jan. 27) 1934.

Rats fed a diet consisting mainly of oatmeal contracted rickets in a more marked degree than did rats which were fed rice. In both diets the absolute values of calcium and phosphorus were made the same, the relation being 4:1. No difference was observed between the intensity of rickets in rats fed a diet in which the rice or the oatmeal had been previously extracted by means of ether and the untreated cereals. The addition of ether rice extract or ether oatmeal extract to the original diets did not perceptibly affect the intensity of rickets. By adding barley extract to the oatmeal diet the development of rickets was markedly checked, as was previously shown by Ruyter de Wildt and Brouwer. Probably barley contains a considerable amount of vitamin D. It is possible that some cereals contain an anticalcifying factor.

van Creveld, Amsterdam, The Netherlands.

Prenatal Conditions

Anomalies of the Interventricular Septum and Pulmonary Orifice. B. Halpert and R. Tennant, Am. J. Path. **10**:375 (May) 1934.

Two cases of an interventricular septal defect with anomalies of the pulmonary orifice and first portion of the pulmonary artery are reported. For details the original article should be consulted.

Moore, New York.

Situs Inversus Viscerum Totalis in Siblings; Case Report. Edward A. Gall and Victor F. Woolf, Ann. Int. Med. **7**:1370 (May) 1934.

Records of only nineteen instances of two or more cases of this condition in the same family were found in the literature, and only fifteen reports of cases in siblings were found. The author reports two additional cases of complete transposition of the viscera in Negro children, who were brother and sister.

Reading, Galveston, Texas.

Agenesia of the Abdominal Muscles in a New-Born Infant. Albert V. Stoesser, Arch. Pediat. **50**:739 (Oct.) 1933.

To the twenty-eight cases of agenesia of the musculature of the abdominal wall already on record the writer adds another and gives references from the literature on this subject.

Waddell Jr., University, Va.

Congenital Cartilaginous Rests in the Neck. Warren B. Matthews, Arch. Surg. **28**:59 (Jan.) 1934.

The case of a 6 year old girl who presented evidence of wryneck is reported. Roentgen examination revealed a lack of normal development of the right half of the body of the first cervical vertebra and nonfusion of the two halves of the second thoracic vertebra, with absence of its posterior spinous process. At operation a button-like nodule with the appearance of cartilage was removed from the right side of the neck. It was thought that the cartilage originated as a remnant of a branchial arch. The condition is described as one of the rarer defects of the branchial system termed congenital cartilaginous rests.

Kaiser, Rochester, N. Y.

Exstrophy of the Bladder (Persistent Cloaca) Associated with Intestinal Fistulas. J. Ross Veal and Elizabeth McFetridge, J. Pediat. **4**:95 (Jan.) 1934.

The authors report the case of a new-born infant who exhibited complicated exstrophy of the bladder associated with fistulas of the intestinal tract (representing

failure of development of the urogenital septum and persistence of the cloaca), absence of the lower intestinal tract and the rectum (representing failure of absorption of the anal membrane), persistence of the postanal gut and spina bifida. Thirty-six cases of congenital malformations of the anus and rectum, described in the records of Charity Hospital in New Orleans, are analyzed from the standpoint of pathology and of mortality.

LeMaster, Evanston, Ill.

Atresia of the Vagina. Arthur M. Dickinson, New York State J. Med. **33**:455 (April 1) 1933.

Two cases of this condition are reported in 15 year old girls, neither of whom had menstruated. In each case an imperforate hymen had caused menstrual blood to accumulate in the vagina until the swelling produced symptoms which suggested pelvic inflammation. With excision of the hymen recovery occurred.

Aikman, Rochester, N. Y.

Treatment of Undescended Testes by Injection of Prolan. Alexander Goldman and Abner Stern, New York State J. Med. **33**:1095 (Sept. 15) 1933.

Two boys, aged 12 and 15 years, respectively, were treated with 100 rat units of extract of the anterior lobe of the pituitary (from the urine of pregnant women) three times a week. There was an increase in the size of the testicles and scrotum, and the boys became more masculine in appearance. The effects of puberty are not considered.

Aikman, Rochester, N. Y.

Lipiodol in the Diagnosis of Congenital Oesophageal Atresia. F. Fraser Brockington and R. Lightwood, Arch. Dis. Childhood **8**:397 (Dec.) 1933.

Iodized poppy-seed oil 40 per cent was injected into the esophagus in two cases of congenital esophageal atresia. In case 1 roentgenograms taken during life showed a blind end to the esophagus, with a little iodized oil in the stomach and lungs. Postmortem examination revealed complete atresia of the esophagus. There was a communication extending from the trachea to the lower portion of the esophagus.

In case 2 roentgenograms taken ante mortem revealed complete atresia of the esophagus. Postmortem injection of the iodized oil into the trachea and esophagus showed no communication. This condition without communication occurs in only 10 per cent of cases of congenital esophageal atresia. Injection of the iodized oil is a valuable diagnostic aid in esophageal atresia.

Kelly, Milwaukee.

Double Aortic Arch. C. E. Snelling and H. Erb, Arch. Dis. Childhood **8**:401 (Dec.) 1933.

A 4 month old girl baby had breathed noisily since birth and had severe spells of blueness during the two weeks previous to examination. There was some regurgitation during and after feeding. Inspiration was difficult. Severe attacks of cyanosis occurred during or following feedings. Barium sulphate was given, and a roentgenogram of the esophagus was taken, which showed a constriction at the third and fourth dorsal vertebrae. There was ballooning of the esophagus below this point. A clinical diagnosis of constriction of the esophagus and trachea by the right aortic arch was made. The infant had an infection of the respiratory tract, contracted bronchopneumonia and died. Postmortem examination revealed that the aorta was divided 3 cm. from its origin. One division passed to the left of the trachea and esophagus and the other division to the right of these structures. The two divisions united again to form the descending aorta. The esophagus and trachea were encircled by this aortic ring. A review of the embryology and recent literature is given.

Kelly, Milwaukee.

PROCESSUS VERMIFORMIS DUPLEX. DAVID M. GREIG, Edinburgh M. J. **41**:277 (April) 1934.

In this critical review of the literature Greig discusses the abnormalities of the appendix, such as congenital absence, embryonic duplication in entirety or presence as a double-barrelled organ with two lumens. Such abnormalities are rare and were not reported in the literature until 1903, after surgical measures attracted increased attention to the organ.

The author mentions the case of Walthard in 1931, that of a girl, aged 7 weeks, in which one vermiform appendix was removed; an umbilical fistula was present also, which when explored was found to contain a branch of the vermiform appendix partly retained in a true developmental umbilical hernia, having been caught in the ligature of the cord at birth.

A valuable enumeration of the literature is appended.

NEFF, Kansas City, Mo.

TWO CASES OF COARCTATION OF THE AORTA. K. D. WILKINSON, Proc. Roy. Soc. Med. **26**:1537 (Oct.) 1933.

Two cases of coarctation of the aorta are reported, the first in a boy, aged 14, and the second in a girl, aged 4.

WILLIAMSON, New Orleans.

CONGENITAL LARYNGEAL STRIDOR; CASE FOR DIAGNOSIS. HAZEL CHODAK GREGORY, Proc. Roy. Soc. Med. **27**:122 (Dec.) 1933.

A baby 8 months old suffered from crowing inspirations. A roentgenogram showed an enlarged thymus, which was treated, with no alleviation of symptoms. By direct laryngoscopy a malformation of the larynx was discovered.

WILLIAMSON, New Orleans.

AN ISOLATED CASE OF CLEIDOCRANIAL DYSOSTOSIS ASSOCIATED WITH HEBRA'S PRURIGO. M. CHEVALLEY and R. GARCIN, Bull. Soc. de pédiat. de Paris **31**:74 (Feb. 21) 1933.

A boy, 4½ years old, had been observed since infancy. Only after he was 4 years old was it noted that both clavicles were almost missing; they were reduced to short stumps corresponding to merely the outer third of the normal-sized clavicle on each side. Cranial abnormalities had been discovered in infancy. These consisted of marked widening of the head, especially of the parietal bones, and delayed ossification of the fontanels. Photographs of the child are reproduced, showing the broad flattened head, the low-set and protruding ears and marked exophthalmos, with the palpebral fissures pointing downward and outward. The shoulders were low and inclined forward; they could easily be held approximated in front of the chest. Roentgenograms of the skull are also included to show marked brachycephaly, with overdevelopment of the middle fossa and shortening of the orbits. The child had suffered from infancy with a rash which was itchy. This would improve for a time, only to return again. Some of these lesions were present on the face, trunk and extremities and showed numerous scratches and excoriations.

BENJAMIN, Montreal, Canada.

ATRESIA OF THE INTESTINE. H. ROUÈCHE, Nourrisson **21**:312 (Sept.) 1933.

An infant apparently normal at birth began vomiting on the second day and passed no meconium. Roentgen and digital examination revealed atresia of the large colon and an obstruction at the lower end of the rectum 2 cm. from the anus. Operation was not permitted; death occurred on the sixth day. Necropsy confirmed the diagnosis.

MCCLELLAND, Cleveland.

HARELIP AND CLEFT PALATE. E. CASELLA, Rev. med., Buenos Aires **19**:119 (Nov.) 1933.

The embryologic and anatomic considerations of these conditions are fully discussed, and many illustrations are given to determine the etiology. The steps in the surgical treatment are described in detail. There are many photographs and colored drawings, and the bibliography is excellent.

SANFORD, Chicago.

INFREQUENT MALFORMATIONS OF THE VERTEBRAL COLUMN AND THEIR INCORRECT DIAGNOSES. M. JACHENS, Arch. f. Kinderh. **100**:98 (Sept. 29) 1933.

Three unusual anomalies of the vertebrae are described. In the first case the condition appeared at first to be a tuberculous gibbus, but was later shown to be spina bifida anterior combined with a Meckel's diverticulum. The second patient appeared to have rachitic kyphosis, but roentgenograms revealed a cleft of the body of the twelfth thoracic vertebra. The third patient was found to have spina bifida occulta combined with a wedge-shaped vertebral anomaly.

LEMASTER, Evanston, Ill.

SEROLOGIC SPECIFICITY OF PLACENTAL TISSUE. G. F. DE GAETANI, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:43, 1932.

Serums of rabbits immunized with an aqueous suspension of human placental tissue reacted with placental extracts and with human red blood cells. The material used for immunization was not free from red blood cells. No attention was paid to the blood group of the persons whose placentas were employed. Some organ specificity was present, as was demonstrated by proper absorption experiments. A few of the serums also reacted with the placenta of the ox. From the fact that the albumin fraction of the antiserums was shown to contain the bulk of the antibodies, Gaetani concludes that the antibodies in the serum were of the Forssman type, but he admits that their source is probably in the red blood cells not removed from the placental tissue. No reaction took place with boiled placental tissue. Immune serums obtained with boiled placental tissue contained species-specific lipoid antibodies.

DAVIDSOHN, Chicago. [ARCH. PATH.]

A CASE OF DOUBLE ESOPHAGUS AND DOUBLE STOMACH. E. GJÖRUP, Acta pædiat. **15**:90 (Nov. 6) 1933.

Gjörup reports the case of a 17 day old girl who was brought to the hospital because of acute abdominal distention and debility. The principal physical finding consisted of two rather prominent masses in the abdomen. The first extended obliquely across the abdomen and suggested a dilated loop of intestine; the second, because of its position and consistency, was thought to be the spleen. Rectal examination showed nothing abnormal. Roentgen studies were not made. Fever and dyspnea developed. Exploratory laparotomy was performed, and the child died during the course of the operation.

Autopsy revealed a double esophagus, both parts of which were patent and both of which communicated with the stomach. The stomach, in turn, was divided into two compartments by an intact septum which allowed no communication between the two chambers. The esophagus on the right led into one of these compartments. Fluid introduced into this tube passed into the stomach and was evacuated through the pylorus. Fluid introduced into the left esophagus entered the stomach, but did not pass into the chamber on the right and could be evacuated only through the esophagus.

The normal topographic relationship between the stomach and the transverse colon was distorted. The pylorus was normal; there was no evidence of tracheobronchial fistula. There was a large subcutaneous abscess on the left side of the

anterior part of the thorax. This extended up into the neck. The left pleural cavity contained a small quantity of purulent fluid, and the right lung had a small amount of fibrin on its surface. The histologic observations were unimportant.

The developmental anomalies of the esophagus most frequently recognized are: agenesis, atresia with tracheo-esophageal fistula, esophago-esophageal fistulas (in which one tube is entirely rudimentary), stenosis and diverticulum. Only two reports of cases in any way comparable with this one have been found in the literature; the similarity is limited.

It is difficult to explain this anomaly on the basis of the usual principles of embryologic pathogenesis. The esophagus develops as a single tube. It does not represent, as do many of the larger vascular trunks, the unique remnant of structures which are transiently paired in the course of their development. The author concludes that the anomaly described indicates an abortive attempt to form a twin. No other evidence of this tendency was discovered either clinically or by pathologic examination.

McCUNE, New York.

CONGENITAL DEFECT OF THE SKULL IN A BABY. A. JONKER, Maandschr. v. kindergeneesk. **3**:80 (Nov.) 1933.

A boy is described who had, associated with hypognathic mandibulae, a large intraparietal fontanel and abnormally wide foramina parietalia; the last-mentioned deviation was congenital and hereditary. The development of the bone was abnormal.

VAN CREVELD, Amsterdam, The Netherlands.

PERSISTENCE OF MECKEL'S DIVERTICULUM. R. J. HARRENSTEIN, Maandschr. v. kindergeneesk. **3**:91 (Dec.) 1933.

Attention is drawn to the dangers which may be caused by a Meckel's diverticulum. Three severe complications are cited as examples. When acute or chronic symptoms of strangulation or rectal hemorrhage occur which cannot be explained in another way, one must always consider the possibility of the persistence of a Meckel's diverticulum.

VAN CREVELD, Amsterdam, The Netherlands.

DEVIATIONS OF EYES AND ORBITS IN ACROCEPHALOSYNDACTYLIA (APERT), DYSOSTOSIS CRANIOFACIALIS (CROUZON) AND TOWER SKULL. P. J. WAARDENBURG, Maandschr. v. kindergeneesk. **3**:196 (Feb.) 1934.

The author summarizes the deformations and anomalies of the height of the skull which may be combined with deviation of the eyes. He reports a case of congenital acrocephalosyndactylia with buphthalmos, combined with a great variety of other hereditary anomalies, and describes a family in which there was acrocephalia for four generations (eight serious cases and five of formes frustes).

The difficulties in the differential diagnosis of dysostosis craniofacialis, dysostosis cleidocranialis and of tower skull are discussed. The necessity of early recognition of mild cases of tower skull and dysostosis is stressed. The article contains a number of good illustrations.

VAN CREVELD, Amsterdam, The Netherlands.

HYPOSPADIA PENIS IN A SINGLE OVUM TWIN. P. A. VOUTE, Nederl. tijdschr. v. geneesk. **77**:2431 (May 27) 1933.

The author reports a case of hypospadia penis in homozygous twins, 7 years old. The cause and development of hypospadia are discussed.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the New-Born

RESUSCITATION AT BIRTH BY EVE'S ROCKING METHOD. NOEL C. FORSYTH, Brit. M. J. **1**:619 (April 7) 1934.

Eve's method of resuscitation is described in this article briefly as follows: The infant is held on the palms of the hands, with the face upward and the legs dangling free, the buttocks being supported and restrained by the first finger and thumb of the left hand, and the head and neck by the first finger and thumb of the right hand. After a few attempts at rocking to and fro, the trunk is covered with a small towel. All this is done before an open fire. The method is apparently based on the theory that the weight of the viscera alternately pushes the diaphragm up and pulls it down. It is considered a scientific, natural and effective procedure by the author.

ROYSTER, University, Va.

ICTERUS GRAVIS NEONATORUM AND ALLIED DISEASES. REGINALD LIGHTWOOD and J. C. HAWKSLEY, Proc. Roy. Soc. Med. **27**:255 (Jan.) 1934.

During the last half century various types of neonatal jaundice have been differentiated. One has been characterized by a familial tendency, an onset within the first forty-eight hours of life and a high mortality. This type, known as icterus gravis, presents important hematologic and pathologic features, which are described. The author made an extensive survey of the literature and found that, with some notable exceptions, pregnancy was normal in this disease and that obstetric difficulties bear no relation to its occurrence. A discussion of the clinical features, diagnosis and treatment is included.

WILLIAMSON, New Orleans.

CEREBRAL HEMORRHAGE IN AN INFANT BORN BY CESARIAN SECTION. H. NERSON, Nourrisson **22**:21 (Jan.) 1934.

A baby was delivered at term by cesarian section on account of a placenta praevia. The baby was easily delivered and appeared normal, but did not breathe and could not be resuscitated. Necropsy revealed a hemorrhage in the posterior horn of the left lateral ventricle. There were no signs of congenital syphilis.

MCCLELLAND, Cleveland.

GENERAL NERVOUS DISTURBANCES IN THE NEW-BORN FOLLOWING DIFFICULT DELIVERIES. M. SCHACHTER, Med. de los niños **35**:70 (March) 1934.

After careful examination the physician can form an idea of the functions of the nervous system in the new-born and in many cases determine what chance the baby has to live after cerebral injury. Cerebral injury accompanying difficult delivery is the greatest cause of death, rather than asphyxia, of which much was said before modern investigations of the changes in the anatomy of the cerebrum caused by difficult birth. The most important of these injuries are ruptures of the large vessels, as they are more exposed to obstetric trauma. Subdural hemorrhage is the most frequent injury; many children die soon after birth of this, and those who succumb in later years from other illnesses frequently show that they had a hemorrhage at birth. The work of Schwartz indicates that 65 per cent of all new-born infants have cerebral hemorrhage.

DWYER, Kansas City, Mo.

DOUBLING OF THE URETER COMBINED WITH STENOSIS AND CALCULUS. H. J. BOEVÉ, Maandschr. v. kindergeneesk. **3**:239 (March) 1934.

A case of this condition in a girl, aged 10 years, is reported. No symptoms were caused by the urinary anomaly.

VAN CREVELD, Amsterdam, The Netherlands.

Acute Infections

UNIMMUNIZED BABY DIES FROM DIPHTHERIA. Health News **10**:29 (Feb. 20) 1933.

The city of Auburn, N. Y., has an enviable record for immunization against diphtheria. Fifty-one per cent of children under 5 years of age have received protection. A child who recently died of diphtheria was the first child to have this disease within four years, and this death represented the first from diphtheria in children since 1928.

AIKMAN, Rochester, N. Y.

CHICKEN POX IN AN EIGHT-DAY-OLD INFANT. WALKER B. HENDERSON, J. Pediat. **4**:668 (May) 1934.

A normal infant on the eighth day of life presented cutaneous lesions; the subsequent course was typical of chickenpox. The infant's mother showed the onset of an eruption of chickenpox on the day of the delivery. One child in the same house had had chickenpox twenty days previously, and another child ten days previously. This is seemingly the earliest instance on record of the occurrence of chickenpox in a normal new-born infant.

LEMASTER, Evanston, Ill.

VALUE OF IMMUNE ADULT BLOOD IN THE TREATMENT OF MEASLES. ALBERT D. KAISER, New York State J. Med. **33**:521 (April 15) 1933.

Two hundred and fourteen children who presumably had been exposed to measles were studied during the epidemic of 1931 in Rochester, N. Y. From 10 to 15 cc. of immune adult whole blood was injected into the gluteal muscles from the third to the seventh day after exposure. It was given on the fourth day, whenever possible.

Of the 214 children, 162 were from families in which measles existed. Of the 162, 40, or 24.5 per cent, failed to contract the disease, while 75.5 per cent contracted it. Of the whole group of 214, 135 contracted measles. Of these, 117 had a modified form; 17 had an average attack, and only 1 had a severe case.

One hundred children who were not given blood were observed in the same families. Of these, 84 had an average attack and 16 a severe form of the disease. Complications were noted in 14 of these children, while similar complications were seen in only 2 of the immunized children.

AIKMAN, Rochester, N. Y.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **49**:677 (June 8) 1934.

For the period of April 22 to May 19 the incidence of measles maintained the highest level in recent years, 124,923 cases being reported. Poliomyelitis also showed the highest incidence in recent years; 146 cases were reported. These were in the Rocky Mountain and Pacific areas. The other areas reported decreases from last year's figures. Scarlet fever showed a decline, and the figures for meningitis, typhoid fever and smallpox were low. The average mortality was 11.8, as compared with 11 for the corresponding period of last year.

SANFORD, Chicago.

FIFTY-ONE STOKES-ADAMS ATTACKS IN FIVE DAYS IN A CASE OF DIPHTHERITIC HEART-BLOCK. J. VINCENT BATES, Brit. M. J. **1**:619 (April 7) 1934.

A case of Stokes-Adams disease is described in which, during the course of a diphtheritic heartblock, fifty-one attacks of syncope were witnessed and recorded in five days. Treatment consisted of frequent injections of epinephrine hydrochloride. The heart made a good recovery, but the patient succumbed to diaphragmatic paralysis.

ROYSTER, University, Va.

THE ANOMALOUS FEATURES OF THE DICK REACTION. J. P. GIBBON, J. Hyg. **34**:30 (Feb.) 1934.

The concept of scarlet fever as an anaphylactic response to a specific antigen (Streptococcus protein) does not necessarily clash with the conception of this disease as a specific toxemia.

One hundred and sixty patients with scarlet fever were tested for cutaneous reactions in each week of the disease. One fourth showed negative reactions in the acute stage. There was a progressive decrease in the number of positive reactions and in the size and intensity of the reactions during the course of the disease, till in the second week two thirds, and in the fourth week nine tenths, of the total number of reactions were negative. Ninety per cent of the original positive reactions became negative with the Dick test, the change occurring more readily in older children. Readings were consistent. Two of the eleven patients who failed to show this change had a relapse. Anomalous features of the Dick test are accounted for. The writer believes that the difficulties are exaggerated, that the allergic conception is not convincing and that one must regard scarlet fever as a specific toxemia.

JANNEY, Wauwatosa, Wis.

BACTERIOPHAGE IN TREATMENT OF DYSENTERY. MISS JAMESSON, J. Indian M. A. **3**:425 (June) 1934.

Cases of bacillary dysentery in which the treatment was with bacteriophage showed 50 per cent less mortality than those in which no such treatment was given, although the convalescence was at times slower. Results in chronic dysentery were not as striking as in the acute form.

TENNEY, Madison, Wis.

STRUCTURAL CHANGES IN ANTIRABIC TREATMENT OF PARALYSIS. S. GETZOWA, G. STUART and K. S. KRIKORIAN, J. Path. & Bact. **37**:483, 1933.

The predominant feature in two cases of Landry's paralysis following antirabic treatment and in one case of unknown origin was a widespread lesion of ganglion cells, inducing rapidly advancing fatal paralysis. The total absence of perivascular zones of demyelinization and perivascular cuffing in the central nervous system argues against the inclusion of antirabic treatment among the somewhat heterogeneous group of factors (smallpox, vaccinia, measles, varicella and typhoid fever) capable of producing acute disseminated encephalomyelitis (Westphal). It also argues against the theory of a virus generally.

[ARCH. PATH.]

RHEUMATIC FEVER FOLLOWING ERYSIPELAS. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **27**:219 (Jan.) 1934.

A girl, 8 years of age, had an attack of chorea in June 1928. Six months later she suffered from an attack of erysipelas of the face, which was followed seventeen days later by a severe attack of rheumatic fever, with arthritis. Four months later epistaxis developed, with tonsillitis. At this time heart disease was discovered.

WILLIAMSON, New Orleans.

ACUTE FATAL DIABETES DURING THE COURSE OF SCARLET FEVER. J. HALLÉ and P. ARONDEL, Bull. Soc. de pédiat. de Paris **31**:101 (Feb. 21) 1933.

A boy, 5 years old, was admitted to the hospital with mild scarlet fever. On the seventeenth day of the disease he became very ill. The urine on admission had been negative for sugar, but after the onset of the acute illness examination of the urine for sugar gave positive results. The ferric chloride test gave negative results. There was no acetone odor of the breath. For two or three days previous to the marked change for the worse the child had an enormous appetite and an unquenchable thirst. He was given repeated injections of insulin and stimulants.

but to no avail. Just before death the urine was free from sugar. The picture described is not that of typical diabetic coma. No blood sugar determinations are mentioned. The father was diabetic.

BENJAMIN, Montreal, Canada.

SERIOUS MENINGEAL DISTURBANCE AT THE ONSET OF VARICELLA. J. HALLÉ and P. ARONDEL, Bull. Soc. de pédiat. de Paris **31**:104 (Feb. 21) 1933.

A boy, 2½ years old, was admitted to the hospital with marked meningeal signs and symptoms. His spinal fluid was normal. The following night the child regained consciousness, and the physical signs, on which a tentative diagnosis of tuberculous meningitis had been made, began to subside. By the next morning he was well, except for some faint cutaneous lesions. These developed into typical lesions of varicella. This disease ran the usual benign course.

BENJAMIN, Montreal, Canada.

SCARLET FEVER. A. SCROGGIE, Arch. de hosp. d. niños, Roberto del Rio **4**:57 (June) 1933.

The author uses the Schultz-Charlton test in the diagnosis of all conditions of the throat that he believes may be due to scarlet fever. Blood taken from the father or mother and given to the child is of great value.

SANFORD, Chicago.

TYPHUS FEVER WITH A SEREMPIONOID ERUPTION. R. INFANTE, Arch. de hosp. d. niños, Roberto del Rio **5**:67 (June) 1933.

The child's temperature was between 39 and 40 C. (102.2 and 104 F.). The eruption was discrete and maculopapular. There were no Koplik spots. Examination of the spinal fluid showed nothing abnormal, and the Wassermann reaction was negative. The Gruber-Widal reaction was negative for paratyphoid fever, but the Weil-Felix reaction was highly positive. There were only 5,300 white cells.

SANFORD, Chicago.

PROPHYLAXIS OF RABIES. J. LUSSICH SIRI, Arch. urug. de med., chir. y especialid. **2**:718 (May) 1933.

The eradication of rabies is difficult in Uruguay because of the resistance encountered by the authorities from the public. The author advocates: the systematic extermination of all stray dogs; a law to enforce the reporting of all cases of rabies; a law to require the muzzling of all dogs and the wearing of a dog collar with the name of the owner on it; international regulation of the transportation of dogs from one country to another, with a quarantine of ninety days; a tax on dogs; the placing of responsibility on the owners of dogs, and the forced vaccination of all dogs against rabies.

HERRON, Spokane, Wash.

MASSIVE HEMORRHAGE FROM THE VESSELS OF THE NECK IN SCARLET FEVER. T. STEIN, Beitr. z. path. Anat. u. z. allg. Path. **91**:202, 1933.

Massive hemorrhage from the vessels of the neck is one of the rarer complications of scarlatina. In six hundred and thirty cases of scarlet fever which came to necropsy in the Wassiljeostrow hospital for infectious diseases of children in Leningrad this complication was the cause of death fourteen times. An additional case from another institution is included. In ten instances the hemorrhage was arterial; in eight of these a careful microscopic examination was made. In five instances the bleeding was of venous origin; a detailed histologic report of four of these is presented. Such hemorrhages are due to destruction of the wall of a vessel by necrosis or acute inflammation, the process reaching the wall from the adjacent diffusely inflamed tissues. In some instances the inflammatory

process that encroached on the wall was gangrenous and appeared to be due to secondary invasion by fusiform bacteria; in other instances streptococci appeared to be the cause of the inflammatory process, which was then more purulent. The internal carotid artery was the site of rupture and hemorrhage in three cases; in these the phlegmon or abscess was retropharyngeal. The external carotid artery was involved in one case and the external maxillary artery in two; in these the abscess was submaxillary. In two cases the common carotid artery, and in three the jugular vein, was the source of the hemorrhage, the abscess being situated in the lateral portion of the neck. Hemorrhage was from the anterior jugular vein in two instances; the abscess was situated in the anterior portion of the neck. In two cases in which the hemorrhage came from an ulcerated, necrotic lesion of the pharynx, the superior laryngeal artery was involved once and the ascending palatine artery once. In half the cases of arterial hemorrhage a single massive bleeding led immediately to death. In the other half the fatal massive bleeding was preceded by one or more smaller hemorrhages. The venous hemorrhages were usually multiple, and death occurred some hours after the terminal massive hemorrhage. In no instance did the fatal hemorrhage occur before the eighteenth or later than the thirty-fourth day of the disease.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

SCARLET FEVER WITH PRIMARY INVOLVEMENT OF THE LUNG. HELENE SSAWRIMOWITSCH, Beitr. z. path. Anat. u. z. allg. Path. **91**:225, 1933.

Although the earliest localization of the disease process in scarlet fever is usually in the pharynx and tonsils, cases in which the primary lesion is in the skin are not unknown, and a few have been reported in which it was in the larynx or the trachea. The author presents three cases in which the diagnosis of scarlatina could not be questioned and in which there was no involvement of the upper air passages except hyperemia of the pharynx. The primary localization was in the lungs, resulting in a necrotizing lobular pneumonia, in which there were many streptococci and relatively few leukocytes. Each lobular area was surrounded by a zone of fibrinous pneumonia and edema. The character of the inflammatory process is held to be identical with that which occurs in the tonsils in the usual case of scarlet fever. Death occurred early, on the second, fifth and seventh days.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

HEMORRHAGIC INFARCTION OF BOTH SUPRARENAL GLANDS IN SEPSIS. S. SCHEIDEGGER, Centralbl. f. allg. Path u. path. Anat. **57**:163, 1933.

A boy, 6½ years old, fell, striking his head on a stone. Meningitis developed within two days, and the boy died shortly after. The periosteum at the site of injury was intact, and there were slight evidences of meningitis. Both suprarenal glands contained free blood, especially in the medulla, and the capillaries contained emboli in which were diplococci and streptococci. Similar organisms were found in the cerebral exudate. Death was due to acute suprarenal insufficiency.

RUKSTINAT, Chicago. [ARCH. PATH.]

SPONTANEOUS RUPTURE OF THE GALLBLADDER IN SCARLET FEVER. H. SSAWRIMOWITSCH, Centralbl. f. allg. Path. u. path. Anat. **58**:49, 1933.

A tear 4 cm. long was found in the gallbladder of a boy, 6 years old, who died on the eighteenth day of scarlet fever. The gallbladder measured 12 by 4 cm., and the tear was on the left side of the fundus. There was no peritoneal reaction to the sterile bile, although rupture of the bladder had presumably occurred some days before death. At the edges of the rent were partially organized thrombi and hyperplastic epithelium. It is supposed that the rupture occurred in a markedly distended organ, because the latter was large, was not inflamed and was ruptured at the fundus. The overdistention is explained on the basis of

paresis of the wall of the bladder due to toxemia. This, coupled with a slight mechanical obstruction to the outflow of bile, such as enlarged lymphatic glands about the duct or some dyskinetic alteration of the sphincter, might lead to rupture.

RUKSTINAT, Chicago. [ARCH. PATH.]

SECOND ATTACKS AND RELAPSES IN THE ACUTE INFECTIOUS DISEASES OF CHILDHOOD. HERMANN ZISCHINSKY, Jahrb. f. Kinderh. **142**:43 (Feb.) 1934.

Götzl (*Wien. klin. Wchnschr.*, 1909, no. 46) described the only proved case of a second attack of measles. Zischinsky observed no second attack and only two relapses in eleven thousand cases. Passive protection lasts fourteen days. Rubeola occurs in several distinct types, each of which probably confers lasting immunity only against the type in question. Second attacks or relapses were not observed in varicella or mumps. Diphtheria confers no immunity; the frequency of the disease in Vienna is so great that second attacks are often observed. One child had six attacks within one and a half years; two sterile cultures were obtained after each. Intervals of from three to six months separated the attacks. Second attacks are often fatal. In any year the ratio of the number of reported cases of diphtheria to the total number of children was found to be equal to the ratio of the number of second attacks to the number of children who had had a single attack. Thirty-one second attacks of scarlet fever were observed, but there were no third or fourth attacks. It is often difficult to distinguish relapses from second attacks. Pospischill believes that pertussis is a chronic disease acquired in early childhood, that the infection persists in the lung for years and that such infections as measles or grip may at any time cause a relapse, with any or all of the typical complications of pertussis. Recurrences, however, are extraordinarily rare.

CLAUSEN, Rochester, N. Y.

EXTRAPHARYNGEAL SCARLET FEVER. A. M. TROIZKAJA-ANDREEWA, Virchows Arch. f. path. Anat. **289**:718, 1933.

Cases of scarlet fever in which the primary localization is in a part of the body other than the pharynx and tonsils have been long known and frequently described as surgical, puerperal and wound scarlet fever. According to the author, histologic study of the primary focus is wanting in most such cases. He therefore presents a detailed histologic study of the local lesion in six of sixteen patients with extrapharyngeal scarlet fever who died in a hospital for infectious diseases of children in Leningrad. In eight of the patients a clinically typical attack of scarlet fever followed burns of the skin. In the remainder the point of entrance was a cutaneous eruption or a slight injury of the skin that became infected. The local lesion was characterized by widespread necrosis and purulent infiltration of the skin and underlying fat. Streptococci were numerous in the inflamed tissues. The regional lymph nodes revealed necrosis and the presence of fibrinous exudate in the sinuses. Whether extrapharyngeal scarlet fever is true scarlet fever must be determined by clinical and epidemiologic considerations. It differs from true scarlatina in no way, except that the period of incubation may be shorter and the mortality higher. Whether a case of scarlet fever is extrapharyngeal in origin must be determined by the absence of acute inflammatory reaction in the tonsils and cervical lymph nodes and by the presence of a necrotizing, purulent process elsewhere.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

ORIGIN OF DIPHTHERIA TOXIN. RICHARD PRIGGE, Ztschr. f. Immunitätsforsch. u. exper. Therap. **77**:421, 1932.

Dried, washed and pulverized diphtheria bacilli have the same toxic effect on guinea-pigs as toxin obtained from cultures. Their toxicity is destroyed by heating at 100 C. and by neutralization with antitoxin. While it was impossible to liberate toxin from the bacilli by means of high pressure, large quantities were liberated by

suspension of the organisms in physiologic solution of sodium chloride. The yield of toxin decreased rapidly with repeated washings, but if the bacterial bodies were left alone for a few days considerable quantities of toxin could again be obtained by washing with physiologic solution of sodium chloride. After repeated washings at proper intervals, the bacterial bodies were found to contain only traces of toxin. The ease with which the toxin passes from the bacterial body into the surrounding medium suggested to Prigge that it is a part of the bacterial body and that after the death of the cell it is liberated gradually with progressive disintegration. Prigge checked and disproved the hypothesis of Dernby and Walbum that the diphtheria toxin is not produced in the bacteria but is a result of the action of enzymes, liberated from dead bacterial bodies, on albumoses and peptones of the medium.

DAVIDSOHN, Chicago. [ARCH. PATH.]

THE INFLUENCE OF HEREDITARY FACTORS IN INFECTIOUS DISEASES. HAGEDOORN-VORSTHEUVEL LA BRAND, Maandschr. v. kindergeneesk. **3**:213 (Feb.) 1934.

Taking mange of the ear in the rat as an example of infectious disease, the author shows that this disease can be looked on as an infectious disease, an avitaminosis or an inherited peculiarity, according to whether one gives most of one's attention to the Sarcoptes mite, the diet or the inherited constitution of the rat. In some cases it can be shown that inherited mendelian factors have a determining influence on infectious diseases. In the author's experiments with mice one mendelian factor protected the animals homozygous or heterozygous for it against septicemia caused by Staphylococcus aureus, which killed all the animals lacking the gene.

In tuberculosis in man the facts parallel the findings in mice. Recent investigations on monozygotic twins confirm these conclusions.

It is indefensible to speak of inherited disease; even when inherited factors play an important rôle, it is possible to modify the other factors so that the hereditary defect is compensated.

VAN CREVELD, Amsterdam, The Netherlands.

CASES OF INFECTION IN MAN CAUSED BY BACILLUS PROTEUS (HAUSER). J. VAN DER HOEDEN, Nederl. tijdschr. v. geneesk. **77**:2407 (May 27) 1933.

From a group of eleven patients (both adults and infants) having agglutinins for Bacillus proteus in the serum, the strain was cultivated from the blood (four times), the cerebrospinal fluid (two times), the empyemic liquid (once), pus from the middle ear (once) and the urine (four times). Sometimes it was uncertain whether Hauser's bacillus provoked the disease or played only a secondary part. The presence of antibodies was strongly in favor of its pathogenicity. One patient with circulating micro-organisms in the blood stream recovered completely. In a case of cystitis due to B. proteus, the reaction of the urine was constantly acid.

Although in most of the patients the serum gave agglutination with the 19 X strain of Weil and Felix, it could easily be distinguished from that of patients with typhoid fever by the coarse type of flocculation and the heat-stable agglutinins (56 C.). (There was one exception.)

In all the cases studied the serums agglutinated the isolated strains of B. proteus in various degrees, with coarse (H) flocculation. Most strains belonged to the species vulgaris.

Nine of the twelve pathogenic strains produced indol, which is contrary to the experience of some previous investigators.

The connection between the fermentation of saccharose and the production of indol was affirmed. Two weak indologenous strains which produced acid, but no gas, from saccharose did not ferment maltose.

VAN CREVELD, Amsterdam, the Netherlands.

Chronic Infections

A Comparison of the Cellular Reaction in Experimental Tuberculosis of the Cornea in Animals of Varying Resistance. Esmond R. Long, Sion W. Holley and Arthur J. Vorwald, Am. J. Path. **9**:329 (May) 1933.

Central interlamellar corneal injections of from 0.01 to 0.005 mg. of moderately virulent bacilli of the human type were made into normal and tuberculous guinea-pigs and normal rabbits and cats, and the lesions were studied. The initial reaction is the outpouring of polymorphonuclear leukocytes, with a gradual replacement by large mononuclears after twenty-four hours. The reaction was most intense in tuberculous guinea-pigs, less so in normal guinea-pigs, still less in rabbits and least in cats, which is in inverse relation to the general resistance of these animals to the strain of tubercle bacillus used.

Moore, New York.

The Origin of the Epithelioid Cell in Experimental Tuberculosis of the Cornea. Esmond R. Long and Sion W. Holley, Am. J. Path. **9**:337 (May) 1933.

Infection of the center of the cornea of a rabbit with tubercle bacilli of human type resulted in a lesion characterized almost solely by polymorphonuclear leukocytes until the arrival of new capillaries, when a rapid replacement of the polymorphonuclears by mononuclear phagocytic cells occurred. When two infecting doses were placed in the same cornea, one at the margin near the normal blood supply and one in the normally avascular center, the replacement of polymorphonuclears by large mononuclears occurred weeks earlier in the lesion close to the limbus.

The mononuclears accounting for this replacement and functioning in the subsequent development of the lesion apparently arose from primitive smaller mononuclear cells present in large numbers in and around the walls of the new capillaries. The source of these cells could not be determined with absolute certainty, but the following observations were evidence that most of them came from the blood stream: (*a*) cells of similar character were present among the erythrocytes in the lumens of blood vessels in great excess of the normal proportion; (*b*) what looked like migration of similar cells could be seen in the walls of the growing capillaries, and (*c*) mitotic figures among them were rare.

After accumulating in and around the capillary walls, the primitive cells underwent progressive transformation by simultaneous increase in size and change of character, without mitosis, into epithelioid cells.

Authors' Summary.

Diagnosis of Surgical Tuberculosis: Comparison of Diagnosis by Inoculation of Guinea-Pigs and by Culture. John E. Blair and Francis A. Hallman, Arch. Surg. **27**:178 (July) 1933.

In order to arrive at a diagnosis of surgical tuberculosis earlier than is possible by the ordinary inoculation of guinea-pigs, the authors studied 150 specimens in a series of parallel diagnostic tests, using inoculations into guinea-pigs and the method of cultivation on crystal violet glycerin water potato medium described by Corper and Uyei. With nontuberculous specimens, such as urine, pus, synovial fluid etc., agreement of culture and animal inoculation was usually obtained. In the tuberculous cases, disagreement occurred in 11.3 per cent, in which the cultures were negative for tuberculosis while gross and histologic examination of the guinea-pigs gave positive results. There is a definite balance in favor of inoculation of animals.

The authors do not believe that the cultural method should replace inoculation into animals in the diagnosis of tuberculosis. It appears to be preferable to include both methods whenever possible. The one serves as a check on the other.

Kaiser, Rochester, N. Y.

CHILDHOOD TUBERCULOSIS. HARRY C. METZGER, J. Michigan M. Soc. **32**:349 (June) 1933.

Metzger outlines a study of tuberculosis in children, as carried on in Wayne County, Michigan. Approximately 12,000 tuberculin tests were made on a group of children of school age 90 per cent of whom were from 5 to 15 years of age. Twenty-five per cent showed a positive skin test, 4.2 per cent of whom showed infection of the bronchial glands on roentgen examination. In 1.3 per cent the condition was classified as "suspicious." Six high school students showed an "adult type" of tuberculous infection and were placed in local sanatoriums for treatment.

CAREY, Detroit.

THE DIAGNOSTIC TUBERCULIN REACTION. JOSEPH GREENGARD and SAMUEL J. NICHAMIN, J. Pediat. **4**:393 (March) 1934.

Six hundred and forty-seven children admitted to Cook County Hospital, Chicago, were tested with an intradermal injection of purified protein tuberculin (0.1 cc. of a 1:100,000 solution of T P T, Seibert), an intradermal injection of 0.1 cc. of a 1:1,000 solution of Koch's old tuberculin, a Pirquet scratch test with undiluted old tuberculin and a dermotubin test over the sternum, using Löwenstein's ointment. The number of children reacting positively to one or more of the tests was 17.1 per cent of those from 6 months to 2 years of age, 21.8 per cent of those from 2 to 5 years of age, 25.7 per cent of those from 5 to 10 years of age and 47.7 per cent of those from 10 to 15 years of age. The highest percentage of positive reactions was obtained with the intradermal tests. With the tuberculin T P T 96.2 per cent of those with positive reactions showed a clearcut positive reaction, while with old tuberculin given intradermally 89.7 per cent of all the reactors gave positive reactions. The dermotubin test showed positive results in 82.1 per cent of all those with positive reactions, while the Pirquet scratch test showed only 65.4 per cent positive results in the total number of those with positive reactions. On the basis of these findings the authors recommend tests with total protein tuberculin (T P T, Seibert) given intradermally for routine use in hospitals. The dermotubin test is recommended for routine use in offices, because of the ease and painlessness of its application. The Pirquet scarification is considered an inferior method.

LEMASTER, Evanston, Ill.

CLINICAL STUDY OF B C G VACCINATION. CAMILLE KERESZTURI, W. PARK, M. LEVINE, P. VOGEL and M. SACKETT, New York State J. Med. **33**:375 (March 15) 1933.

More than 1,000 cases have been studied. Within five years 413 babies received B C G. The authors conclude that it is harmless, and that vaccinated children show a lower mortality from tuberculosis than unvaccinated children.

Eighty-four per cent of the children who were vaccinated parenterally gave positive reactions to tuberculin, whereas only from 40 to 50 per cent of those vaccinated orally gave positive reactions. As a whole, the children vaccinated parenterally with B C G showed the lowest mortality from tuberculosis of all the groups.

AIKMAN, Rochester, N. Y.

SANOCRYSIN IN TUBERCULOUS MENINGITIS. T. B. BROADWAY, Brit. M. J. **2**:972 (Nov. 25) 1933.

A patient with a condition which was diagnosed as tuberculous meningitis was treated with intravenous and intrathecal injections of sodium aurothiosulphate. There was prompt improvement, and the child remained in a good condition, but collapsed seven hours before death.

ROYSTER, University, Va.

IMPRESSIONS FROM A RECENT PERSONAL STUDY OF TUBERCULOSIS WORK IN THE UNITED STATES. D. MELVILLE DUNLOP, Edinburgh M. J. **41**:188 (March) 1934.

The author states that the two most interesting pieces of epidemiologic research that he saw in America are those being carried out at Baltimore and the village of Saranac Lake.

In Baltimore all children under 2 years of age from a tuberculous household who were reactors are carefully observed. Serial roentgen films and the child's condition are watched, so that within twenty years much knowledge of the natural history of the disease may be obtained. The survey has shown thus far that in infants with a tuberculin-positive reaction a 30 per cent mortality is found, which is not indicative of a rapidly fatal prognosis.

In the village of Saranac Lake each child has frequent clinical and roentgen examinations up to adult life. This does not include tuberculin tests, because of the lay prejudice to such a procedure.

The occurrence of a positive tuberculin reaction causes American physicians to hunt diligently for a primary tubercle in the lung, although other lymphatics, such as the pharyngeal lymph nodes, in the author's opinion, might more conveniently be the early resting-place for the micro-organism.

NEFF, Kansas City, Mo.

MODERN CONCEPTIONS OF HEREDITARY SYPHILIS. M. CARLE, Ann. de dermat. et syph. **4**:106 (Feb.) 1933.

Syphilographers are now almost unanimous in the opinion that the mother of a new-born syphilitic baby is always syphilitic, and that her seeming ability to nurse such an infant with impunity is due to the fact that she is "protected by her own syphilis"; they also believe that an infant born of a syphilitic mother is habitually syphilitic, in spite of appearances of health.

A few authorities admit the occasional possibility of an inheritance of syphilitic contamination directly from the father, but all recognize that this is rare. Carle believes that paternal transmission of the spirochete to the ovum does not occur.

The presence of the spirochete in the semen does not by any means favor the possibility of paternal transmission. The semen is a complex fluid into the composition of which secretions from several different sources enter (e. g., prostate and seminal vesicles). A syphilitic lesion of one of these organs easily explains the presence of the spirochete in the semen, and this readily accounts for the frequency of chancre on the vagina and cervix, at the same time refuting the idea of conceptional syphilis of paternal origin.

There is no possible explanation of paternal transmission except a supposition that the spirochete, lodged in the spermatozoon, penetrates with it into the ovum. Two objections to this theory are apparent. First, the spirochete is three or four times larger than the head of the spermatozoon, and there is no record of any one ever having seen the one in the other. Second, it seems inconceivable that the infection of the spermatozoon, transmitted to the ovum in turn, could permit the development of so delicate an organism as the fetus.

Of course, it has been postulated that the spirochete may penetrate the spermatozoon in an ultramicroscopic granular form and subsequently undergo normal development. But it is far more logical to assume that the spirochete infects some point in the maternal genitals, perhaps at the same time that the spermatozoon fertilizes the ovum, whereupon the contaminated mother transmits the disease to the fetus by the hematogenous route.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

A Rare Case of Congenital Neurosyphilis. M. Gerbasi, Pediatria **41**:900 (July 1) 1933.

The author reports and discusses fully a case of hereditary neourosyphilis in which the symptoms of disseminated myelitis were associated with an adiposo-genital syndrome.

Signorelli, New Orleans.

Specificity of Allergic Tuberculin Tests. Emilio Pezza, Pediatria **42**:132 (Feb. 1) 1934.

In this article the author reports studies undertaken for the purpose of determining the relation between the cutaneous absorptive capacity and tuberculin tests. Note was made of the time of disappearance of the cutaneous elevations resulting from the McClure and Aldrich test.

The tests were not found to be necessarily dependent on each other, for there was no consistent decrease in the time of disappearance of the cutaneous elevation caused by saline solution, while the cutaneous allergic tuberculin reaction was slight or absent.

Signorelli, New Orleans.

Parrot's Disease. R. Cibils Aguirre and R. A. Tetes, Arch. argent. de pediat. **3**:784 (Dec.) 1932.

The authors report a typical case of this condition in an infant 3 months old. Both osteochondritis and periostitis were present. The osteogenic lesions manifest themselves in diminished activity of the osteoblasts, alteration in the development of the cartilage and a disturbance in the normal reabsorption. Fundamental intracellular substances proliferate and calcify. There is deficient formation of subchondral trabeculæ. These changes lead to abnormal processes of absorption and eventual formation of connective tissues. Disturbances of growth appear, and there is excessive osteoclastic activity.

Schultz, Chicago.

Insidious Initial Forms of Tuberculosis in the Infant. Gustavo Cardelle Penichet, Bol. Soc. cubana de pediat. **5**:59 (March) 1933.

These forms of tuberculosis are characterized by extremely mild symptoms such as low grade fever, anorexia, gastro-intestinal and nutritional disturbances, anemia and cough. Physical examination of the chest revealed nothing abnormal. Four fundamental factors are of help in establishing the diagnosis of this not infrequent condition: a painstaking, minute history, a positive reaction to the Mantoux or Pirquet tuberculin test, the finding of the Koch bacillus in the sputum or the gastro-intestinal contents and the roentgen findings.

Schlutz, Chicago.

Therapeutic Indication of Pneumothorax and Certain Curable Forms of Tuberculosis in Children. René Garcia Mendoza, Bol. Soc. cubana de pediat. **6**:7 (Jan.) 1934.

The author points out the difficulties in differentiating pulmonary epituberculous infiltrations from true tuberculous lesions in the lung. It is not easy to determine when a tuberculous lesion becomes caseous. Roentgenography is of some help. Examination of the sputum almost uniformly gives negative results. The author places the greatest reliance on careful physical examination and the character of the râles and breath sounds. It is the caseating type of tuberculosis for which pneumothorax and collapse of the thorax are recommended, particularly if the process is unilateral. In a certain number of these cases the condition clears up without any intervention, such as pneumothorax. The author reports a few illustrative cases.

Schlutz, Chicago.

PROPHYLAXIS OF CONGENITAL SYPHILIS. T. VALLEDOR, Bol. Soc. cubana de pediat. **6**:23 (Jan.) 1934.

The author's program for the prophylaxis of syphilis comprises the following points: (1) A preconceptional prophylaxis of syphilis, which begins at the time of the marriage of syphilitic persons, (2) active treatment of the pregnant syphilitic mother, (3) maternal nursing or breast feeding for the congenitally syphilitic infant, (4) early and intensive treatment of the congenitally syphilitic child and (5) the organization of properly conducted dispensaries and the necessary intelligent social service supervision.

These five points are elaborated in great detail. There can be no doubt of the efficacy of this program in curbing the spread of syphilis and modifying the influence on the population of this great social disease. The author considers the widespread organization of dispensaries one of the most effective measures.

SCHLUTZ, Chicago.

SUBCUTANEOUS VACCINATION OF CHILDREN WITH B C G. ERNESTO SELVA SANDOVAL, But. Soc. catalana de pediat. **4**:135 (July-Sept.) 1931.

In a detailed study of the vaccination of seventeen children with B C G, the author found lymphocytic leukocytosis, with a shift in the Arneth count to the left. He advises against giving the vaccine parenterally to artificially fed children under 1 month of age during hot weather. If this precaution is taken, the vaccine in small and large doses is effective; there are no general reactions, and the local reactions are few.

WATSON, Elmhurst.

EPICRANIAL PHLEBOSCLEROSIS OF THE INFANT, AN INFREQUENTLY RECOGNIZED SIGN OF CONGENITAL SYPHILIS. PEDRO PARDO, Pediatría españ. **22**:592 (Sept.) 1933.

Epicranial phlebosclerosis in an infant under 1 year of age is a symptom of congenital syphilis. It is a common sign, but is often overlooked.

Histopathologically, epicranial phlebosclerosis is a degenerative syphilitic phlebosclerosis similar to chronic sclerosing phlebitis.

SCHLUTZ, Chicago.

FREQUENT COEXISTENCE OF PULMONARY LESIONS WITH OTHER TUBERCULOUS SEQUELAE. A. AMORIM, Pediatria, Rio de Janeiro **1**:47 (March) 1934.

Ten roentgenograms of pulmonary lesions due to tuberculosis in children with various types of tuberculosis of the bone are shown.

SANFORD, Chicago.

GENESIS OF ACUTE, GENERAL, MILIARY TUBERCULOSIS. I. MINGUEZ, Beitr. z. Klin. d. Tuberk. **82**:84, 1933.

This study is based on thirty-nine autopsies. In each Minguez searched for the focus of the spread, using as criteria Loeschcke's postulates: liquefaction of contents, presence of a large number of bacilli and presence of blood as an indication of rupture into a blood vessel. He believes that endovascular tubercles are the result and not the cause of bacillemia. In thirty-one cases such foci were certainly demonstrated, and in eight doubtfully so. The focus was in a lymph node in twenty-two instances; it was primary three times; it was in a caseated testicle once, and in the remaining three cases it was indeterminate.

MARGULIS, Tucson, Ariz. [ARCH. PATH.]

DOES THE TREATMENT OF CONGENITAL SYPHILIS PREVENT THE DEVELOPMENT OF INTERSTITIAL KERATITIS? INTERSTITIAL KERATITIS AFTER INJURY. K. VOM HOFE, Klin. Monatsbl. f. Augenh. **90**:492 (April) 1933.

In four cases reported by vom Hofe early treatment of congenital syphilis did not prevent later development of interstitial keratitis. Two of the patients, aged

11 and 13, had received antisyphilitic treatment in infancy; one, aged 12, had had such treatment about nine months prior to observation, and the fourth patient, aged 25, at the age of 14 years, after interstitial keratitis had developed. A recurrence followed in one eye two days after a small foreign body became embedded in the cornea. Numerous deep-seated vessels developed at the site of the foreign body, and parenchymatous cloudiness in its surroundings at a considerable distance. The cornea was fairly clear again a month later.

STOLL, Cincinnati. [ARCH. OPHTH.]

TREATMENT AND PROPHYLAXIS OF CONGENITAL SYPHILIS. EINAR HVAL, Norsk mag. f. lægevidensk. **95**:241 (March) 1934.

The author considers the antepartum treatment of the mother the most valuable means of combating congenital syphilis. The result of the combined treatment of the infant with bismuth and neoarsphenamine is good. In the cases reported the author emphasizes the importance of the antenatal treatment. The fact that there were twenty-five new cases of congenital syphilis within one year in the city of Oslo (two hundred and seventy-thousand inhabitants) shows that the antenatal prophylactic treatment is not sufficiently understood as yet.

TOVERUD, Oslo, Norway.

Internal Diseases

RHEUMATIC MANIFESTATIONS IN SUBACUTE BACTERIAL ENDOCARDITIS IN CHILDREN. O. SAPHIR and S. A. WILE, Am. Heart J. **9**:29 (Oct.) 1933.

The authors report a clinical and pathologic study of ten cases of subacute bacterial endocarditis, eight occurring in children and two in young adolescents who had been under observation since childhood. In every case there was a history of preceding rheumatic infection. On postmortem examination all hearts showed healed endocarditis, subacute bacterial endocarditis and Aschoff bodies in the heart muscle. Blood cultures yielded Streptococcus viridans.

In discussing the relationship between the rheumatic infection and the subacute bacterial endocarditis, they point out that a coincidence of the two conditions would be most unlikely. Moreover, they bring forth evidence to show that rheumatic infection and subacute bacterial endocarditis are different diseases, rather than merely different manifestations of the same disease, and that the injury of a previous rheumatic infection predisposes the valve to a subsequent bacterial endocarditis.

GIBSON, Chicago.

PERSISTENCE OF IMMUNITY AFTER THE ABOLITION OF ALLERGY BY DESENSITIZATION. ARNOLD R. RICH, FREDERICK B. JENNINGS JR., and LILLIAN M. DOWNING, Bull. Johns Hopkins Hosp. **53**:172 (Oct.) 1933.

With Pasteurella aviseptica and Pneumococcus as the infecting organisms, experiments were carried out in order to determine whether immunity would be less efficient after the abolition of allergy by desensitization. When the capacity for reacting with allergic inflammation is completely destroyed by the injection of large doses of killed bacteria into the veins of hypersensitive, immune animals, immunity to intracutaneous infection with millions of lethal doses of living, virulent bacteria remains intact. Inflammation at the site of infection in such animals is far less in amount than in untreated, allergic, immune animals—far less, indeed, than in normal controls; but the bacteria are prevented from spreading from the site are as effectively destroyed as they are in the allergic, immune body. The immune state acts to enhance so greatly the protective power of the inflammatory mechanism that much less, rather than much more, inflammation is required to protect the body from infection. Damage to tissue at the site of infection is also far less in the desensitized than in the allergic animals.

Even in the highly allergic, immune body, therefore, allergic inflammation is not necessary for protection against infection, and in its absence the body is protected with much less damage to tissue than occurs in the allergic body.

AUTHORS' SUMMARY.

HYPERINSULISM. RUSSELL M. WILDER, Internat. Clin. **2**:1 (June) 1933.

Hyperinsulinism is characterized by attacks of faintness, numbness of the tongue and lips, weakness, profuse perspiration, trembling, intense hunger, loss of consciousness and, occasionally, convulsions. It may be confused with epilepsy. The blood sugar is low, but an inconsistency exists between the intensity of the reaction and the blood sugar values. Tumors of the pancreas were found in fifteen of twenty-nine cases studied and hypertrophy of the islands of Langerhans in fifty-one. The treatment consists in frequent feeding of a diet low in carbohydrate and high in fat. Surgical intervention has been successful in a few cases.

MILLER, South Bend, Ind.

RENAL RICKETS. A. R. ELLIOTT, J. A. M. A. **100**:707 (March 11) 1933.

There is a form of rickets which develops in childhood in association with, and apparently caused by, persistent renal insufficiency. Bodily development is greatly retarded, and sexual infantilism may exist. The blood reveals an increasing azotemia coinciding with the increasing excretory inadequacy of the kidney. The blood pressure is not elevated until perhaps just before death. Death results from renal insufficiency. Roentgenologically the bony structures disclose typical rickets, with genu valgum as the outstanding manifestation. BONAR, Salt Lake City.

STUDIES IN CRETINISM AND HYPOTHYROIDISM IN CHILDHOOD. I. P. BRONSTEIN, J. A. M. A. **100**:1661 (May 27) 1933.

The average cholesterol content of the blood of twenty-five normal children was 190 mg. plus per hundred cubic centimeters. Hypercholesteremia ranging from 277 to 782 mg. per hundred cubic centimeters was found in twelve children with thyroid deficiency. In these cases thyroid therapy lowered the blood cholesterol, raised the basal metabolic rate and effected clinical improvement. The use of the blood cholesterol as an index to thyroid dosage seems desirable.

BONAR, Salt Lake City.

CHRONIC NONSPECIFIC NEPHRITIS. C. A. ALDRICH and H. H. BOYLE, J. A. M. A. **100**:1979 (June 24) 1933.

The term "chronic nonspecific nephritis" is used to denote a clinical group characterized by: (1) edema; (2) arterial hypertension; (3) increase in the nonprotein nitrogenous constituents of the blood; (4) hematuria; (5) marked albuminuria; (6) cylindruria, and (7) a rapidly fatal or chronic course. It is suggested that this type of nephritis is due to hygienic or dietary rather than to bacterial causes, and that infection may be the result of the disease rather than the cause. In view of the fact that diets low in protein and salt were futile, it was decided to institute diets high in protein and vitamins and to improve the hygiene. No elevation of the blood pressure or increase of the nonprotein nitrogenous constituents of the blood appeared in the group as a whole. The majority of the patients have shown definite improvement, and the death rate has decreased.

BONAR, Salt Lake City.

SYSTOLIC MURMURS IN CHILDREN. C. R. MESSELOFF and E. T. OPPENHEIMER, J. A. M. A. **101**:17 (July 1) 1933.

Various diagnostic criteria are used to differentiate between organic and functional murmurs. A functional murmur is invariably systolic, heard only in the early part of systole, very short and blowing, heard best over the pulmonic area and rarely transmitted beyond the precordium. It may vary with change of position, exercise or respiratory movement. Sixty-four children with systolic murmurs, both organic and functional, were studied clinically and phonocardiographically. Eighty-six per cent of the cases of functional murmur presented high pitched vibrations only, while cases of organic murmur revealed low as well as high pitched vibrations. This suggests an additional aid in the differentiation of these two conditions.

BONAR, Salt Lake City.

HEREDITARY GAUCHER'S DISEASE. J. P. ANDERSON, J. A. M. A. **101**:979 (Sept. 22) 1933.

Gaucher's disease is considered familial but nonhereditary. A family is reported in which there is a possibility of hereditary transmission of this disease. It has affected nearly all the females and none of the males. In the first generation there were three possible cases, in the second none and in the third one possible case, two probable and two proved cases.

BONAR, Salt Lake City.

CHRONIC PEPTIC ULCER IN CHILDHOOD. CHARLES STANLEY WHITE, J. Pediat. **3**:568 (Oct.) 1933.

Two cases of chronic peptic ulcer in girls, aged 15 and 7, are reported. One patient recovered following surgical intervention and the other showed relief of symptoms on a diet of the Sippy type. White emphasizes the importance of melena as a symptom and the necessity of roentgen examination in suspected cases. Clinical research on dyspeptic conditions in childhood is urgently needed and might add considerably to the present knowledge of peptic ulcer in childhood.

LEMASTER, Evanston, Ill.

VIRILISM AND HYPERTENSION IN INFANCY ASSOCIATED WITH ADRENAL TUMOR. FRANK VANDER BOGERT, J. Pediat. **3**:629 (Oct.) 1933.

A case of carcinoma of the suprarenal gland in a girl, 2 years old, is reported. The findings were obesity, precocious development, hirsuties, change of voice, virilism, marked hypertrophy of the clitoris and external genitalia, hypertension and cardiac enlargement. At operation the right suprarenal gland, which was larger than the left, was removed subcortically. Histologic sections revealed carcinoma. The patient died thirty-six hours after the operation.

LEMASTER, Evanston, Ill.

IDIOPATHIC DILATATION OF THE COMMON BILE DUCT IN CHILDREN. ROBERT E. GROSS, J. Pediat. **3**:730 (Nov.) 1933.

Fifty-two cases of idiopathic choledochus cyst in childhood are thoroughly reviewed and analyzed, and two additional cases are reported. The essential finding is a large cystic dilatation of the common bile duct. In about half of the cases some obstruction of the bile duct distal to the cystic enlargement was found. The cystic dilatation seems probably to be due to a congenital weakness of the wall of the duct plus obstruction to the free flow of bile. The chief signs are abdominal pain, abdominal tumor and jaundice with acholic stools at intervals. The accepted form of treatment is to anastomose the biliary and intestinal tracts at one operation.

LEMASTER, Evanston, Ill.

CARCINOMA OF THE RECTUM AND SIGMOID WITH PARTICULAR REFERENCE TO THE DISEASE AS SEEN IN YOUTH. WILLIAM M. SHEDDEN, New England J. Med. **209**:528 (Sept. 14) 1933.

The incidence of malignant epithelial neoplasm in youth (less than 20 years of age) is probably under 4 per cent of the entire incidence of neoplastic disease and that in persons between 20 and 35 years is about 7 per cent. It is common to have death supervene in from six months to a year after the onset of symptoms, as in childhood and, to a lesser degree, in young adult life it is a fulminating disease. The youngest girl was 11 years old; a report of her case was published by Stern in 1892. The youngest males were two boys, each aged 9; a report of one of the cases was published by Steiner in 1865. This article concerns a group of thirty-six patients under 20 years of age and another group of twenty-four patients between the ages of 20 and 35. In the youthful group (under 20 years) the symptoms in order of frequency were: abdominal pain in 20 (55 per cent); rectal bleeding in 11 (30 per cent); constipation in 11 (30 per cent); rectal pain in 8 (22 per cent); frequent stools in 7 (19 per cent).

The younger the patient the greater the tendency to a highly malignant process. Diagnosis by biopsy prior to instituting therapy is always advisable. Periodic rectal examinations must be made, as 87 per cent of the rectal and sigmoid growths in this series were within reach of the finger. The therapy of choice is the radical operation; colostomy, as an adjunct, is always necessary.

GENGENBACH, Denver.

DIAPHRAGMATIC HERNIA AND SECONDARY ANEMIA; TEN CASES. A. V. BOCK, J. W. DULIN and P. A. BROOKE, New England J. Med. **209**:615 (Sept. 28) 1933.

While all the cases reported were of adults, the observation of the authors that secondary anemia was an outstanding symptom, owing to the recurrent attacks of hematemesis, with an absence of other physical signs of gastric disturbances, is worthy the attention of pediatricians in treating congenital cases.

GENGENBACH, Denver.

ESTRIN THERAPY IN A CASE OF HEMOPHILIA. ROBERT L. BROWN and FULLER ALBRIGHT, New England J. Med. **209**:630 (Sept. 28) 1933.

After a thorough study of an adult with hemophilia, the authors concluded that the presence of estrin in the blood stream, presumably in amounts far greater than are found in normal women as judged by the urinary excretions, did not in itself alter the coagulation time in a case of hemophilia.

GENGENBACH, Denver.

THYROID DISORDERS IN CHILDHOOD. RICHARD B. CATTELL, New England J. Med. **209**:867 (Nov. 2) 1933.

Approximately 1 per cent of the patients presenting disorders of the thyroid gland who come to the Lahey Clinic are under 13 years of age. These disorders in infancy and childhood may be roughly divided into those that are developmental in origin, those that are functional and those that are of a neoplastic type.

Congenital absence of the thyroid gland is very rare and is inconsistent with life. There were three patients with a completely lingual thyroid present since childhood. Thyroglossal cysts, sinuses and fistulas are not rare. There were eleven cases in patients under 20 years of age. "Complete excision of the cyst or sinus together with removal of the central portion of the hyoid bone and a core of the muscles in a line up to the foramen cecum 'en bloc' after the method of Sistrunk, is essential to effect a cure."

Colloid goiter is the most frequent disorder of the thyroid in children. The treatment of colloid or adolescent goiter should be conservative. It should be appreciated, however, that when colloid goiter persists it is the first stage in the production of endemic or adenomatous goiter. Hyperthyroidism may occur at any age after 2 years. In its clinical and pathologic manifestations it is similar to the disease seen in adults. "In the absence of an elevated metabolism in these children we do not make the diagnosis of hyperthyroidism. . . . With the diagnosis established we believe all of these children should be operated upon.

"We do not believe x-ray therapy should be employed since it is too difficult to gauge with sufficient accuracy to get relief and not get hypothyroidism." Children are given preoperative treatment until they show a satisfactory gain in weight. It is best to divide the operation into two stages. Between stages six weeks are allowed to lapse, during which the patients are given 5 drops or less of compound solution of iodine, a day. The results of the operation are very satisfactory. There was no instance of postoperative parathyroid tetany.

Thyroiditis is very rare in children. Mild degrees of inflammation with local tenderness may at times be demonstrated, associated with tonsillitis, cervical adenitis and generalized infections. The condition does not require treatment. The only benign tumor of the thyroid is the discrete adenoma. "It is a rare finding in children and in our experience has been encountered only three times." The treatment should be surgical intervention at any age. Lateral aberrant thyroid tumors may occur at any age, although but two occurred in children (11 and 13 years of age). The treatment is local excision of the discrete tumors, and block dissection of the neck when they are multiple. There were three cases of carcinoma of thyroid origin in children. They occurred at the ages of 6, 11 and 13 years. The first child has remained free from recurrence for eighteen months since operation. The second has remained free from recurrence for over two years. In the third case a large amount of the malignant tissue was excised and tracheotomy done. With roentgen treatment evidence of the tumor disappeared and the child appeared well for nine months; after this the tumor recurred rapidly and caused death in thirteen months.

GENGENBACH, Denver.

INCIDENCE AND CLINICAL SYMPTOMS OF MINOR RESPIRATORY ATTACKS WITH SPECIAL REFERENCE TO VARIATION WITH AGE, SEX, AND SEASON. SELWYN D. COLLINS and MARY GOVER, Pub. Health Rep. **48**:1155 (Sept. 20) 1933.

Records of the incidence and clinical symptoms of respiratory disease were obtained by semimonthly reports on 2,998 persons in the families of medical officers of the United States Army, Navy and Public Health Service and the faculty members of certain universities over a period of thirty-three months ending in June, 1926. Data were also collected from 1,872 college students during 1924. The annual incidence of respiratory disease in the family group was 1,851 cases per thousand or nearly 2 cases per person per year. About half of the cases were reported as head colds only; a fourth of the cases were described as influenza, sore throat or bronchitis, while the remaining fourth were reported as combinations of two or more of these conditions. For the students, the annual incidence of respiratory disease was 3,333 per thousand, or more than 3 cases per person per year. Nearly three fourths of the cases were reported as head colds only. Of thirteen symptoms on which information was obtained, constipation, nasal obstruction and expectoration were the only ones to show much difference in the sexes, and these occurred with greater frequency among males than among females. The incidence of coryza has its peak in the fall. The incidence of influenza is low in the fall and highest in the late winter and spring. Bronchitis and sore throat lie between these extremes.

LEMASTER, Evanston, Ill.

ANAEMIA IN CHILDHOOD: PART IV. THE HAEMOLYTIC (ERYTHRONOCLASTIC) ANAEMIAS OF THE NEONATAL PERIOD; WITH SPECIAL REFERENCE TO ERYTHROBLASTOSIS OF THE NEW BORN. L. G. PARSONS, J. C. HAWKSLEY and R. GITTINS, Arch. Dis. Childhood **8**:159 (June) 1933.

Hemolytic anemias of the new-born are grouped as (*a*) with hydrops foetalis, (*b*) with icterus gravis and (*c*) without edema or icterus gravis. These groups are described clinically, and pathologic changes found in association with each group are given. The view is put forward that the embryonic erythropoiesis present in them is a result and not a cause of these anemias. It is suggested that the term "erythronoclastic anemia" is more correct, as very often there is destruction or paralysis of the hemopoietic centers as well as destruction of red cells in the blood stream (hemolysis).

KELLY, Milwaukee.

ANAEMIA IN CHILDHOOD: PART V. THE HAEMOLYTIC (ERYTHRONOCLASTIC) ANAEMIAS OF LATER INFANCY AND CHILDHOOD; WITH SPECIAL REFERENCE TO THE ACUTE HAEMOLYTIC ANAEMIA OF LEDERER AND THE ANAEMIA OF VON JAKSCH. L. PARSONS and J. C. HAWKSLEY, Arch. Dis. Childhood **8**:184 (June) 1933.

These destructive anemias (erythronoclastic) of later infancy and childhood are divided into four groups: (1) acute hemolytic (Lederer type); (2) subacute hemolytic anemia; (3) von Jaksch's syndrome, and (4) acholuric jaundice. Nine cases of the first group are described. The onset is very sudden, apparently infectious, and the anemia severe. Eight patients recovered and one died. The subacute cases are less sudden in onset. It is recommended that the title "von Jaksch's anemia" be discarded, as the syndrome is a chronic form of hemolytic anemia.

KELLY, Milwaukee.

ANAEMIA IN CHILDHOOD: PART VI. NUTRITIONAL ANAEMIA IN MOTHER AND CHILD. A. V. NEALE and J. C. HAWKSLEY, Arch. Dis. Childhood **8**:227 (Aug.) 1933.

The biologic problems discussed in this paper once more emphasize the value of adequate infantile storage of iron, etc., at birth and the importance of a mixed diet at least after the first nine months of life. Anemia in pregnancy may have far-reaching effects on the fetus. The transference of hemopoietic substances from mother to fetus is progressive throughout pregnancy and is considerably increased in the late weeks. Treatment in cases of infantile anemia due to the maternal state is highly successful. Several cases are cited of anemic mothers treated with iron and yeast. The blood counts were markedly improved. The infants had normal blood pictures.

KELLY, Milwaukee.

ANAEMIA IN CHILDHOOD: PART VII. MONOCYTIC REACTION IN MYELOSIS. R. GITTINS and J. C. HAWKSLEY, Arch. Dis. Childhood **8**:241 (Aug.) 1933.

A detailed report is given of prolonged monocytosis in a child. This condition was incidental in the course of chronic myelosis, as revealed by autopsy. Leukemic reticulo-endotheliosis is discussed.

KELLY, Milwaukee.

ANAEMIA IN CHILDHOOD: PART VIII. LEUKEMIA (LEUCOSIS) IN CHILDREN. R. GITTINS, Arch. Dis. Childhood **8**:291 (Oct.) 1933.

The report of a study of fourteen cases of leukemia in children is presented. The clinical description, blood pictures and postmortem observations are given. All the cases were acute. There were eleven cases of the lymphatic, two of the myeloid and one of the monocytic type.

Although certain features of myelosis can be imitated by severe myeloid reaction in inflammatory disease, the profound anaplasia of myelosis, often obliterating

all erythropoietic function, is an outstanding feature. Lymphadenosis is not imitated by any known process of infectious disease in man. The impression left, after cytologic and histologic study, is uniformly that leukosis is a neoplastic process. Leukocytosis and leukosis appear to be respectively hyperplastic and neoplastic phenomena and analogous to reparative processes and malignant focal new growths.

KELLY, Milwaukee.

COELIAC DISEASE. R. E. STEEN, Brit. J. Child. Dis. **30**:163 (July-Sept.) 1933.

This article consists of a report of two cases of celiac disease, with a general discussion of the symptomatology. In order to make a diagnosis at least two of the four features of the disease must be present: (1) large abdomen; (2) large, pale, offensive stools; (3) failure to gain weight and delayed physical development; (4) characteristic mentality. In regard to prognosis, Steen believes that as long as the matter is still undecided it is best to take a hopeful outlook. Leonard Parsons states that celiac disease rarely persists into adult life, whereas Izod Bennett holds the opposite view.

The treatment is chiefly dietetic, the diet being, as far as possible, fat-free, i. e., consisting chiefly of protein with "for preference, starch in the form of dextrimaltose." Skimmed milk is used. The importance of supplementing the diet with vitamins A and D is stressed. This is best accomplished by using one of the vitamin concentrates. Steen believes that most cases of celiac disease are best treated in an institution, as a disciplined and ordered life can be carried out more effectively there than at home.

LANGMANN, New York.

A RARE PRIMARY OSSEOUS DYSTROPHY. PHILIP ELLMAN, Brit. J. Child. Dis. **30**:188 (July-Sept.) 1933.

A 15 year old boy showed great distortion of the trunk and extremities. There were swelling and limitation of movement of almost all the joints and a considerable degree of generalized muscular wasting. On roentgen examination all the bones showed marked evidence of osteoporosis, the epiphyseal ends were enlarged while the shafts of the long bones were attenuated. The heads of the femurs were considerably distorted and there was marked irregularity of the articular cartilage. The tibias, metacarpals and phalanges also showed abnormalities. The blood calcium, phosphorous and phosphatase were low.

The case is similar to two described by Morquio and one by Mayer and Brennemann.

LANGMANN, New York.

CIRRHOSIS OF THE LIVER IN A BABY. BRYAN WILLIAMS, Brit. M. J. **1**:850 (May 12) 1934.

The author reports a case of cirrhosis of the liver in a baby.

ROYSTER, University, Va.

CLINICAL AND EXPERIMENTAL INVESTIGATION INTO THE ETIOLOGY OF THE INFANTILE CIRRHOSIS OF THE LIVER. S. C. LAHIRI, Calcutta M. J. **27**:439 (June); **28**:22 (July) and 57 (Aug.) 1933.

Infantile hypertrophic biliary cirrhosis, when fairly advanced, is characterized by a hard, enormously enlarged liver, various gastro-intestinal symptoms, from mild to moderate fever, enlargement of the spleen and eventually, in unfavorable cases, signs of portal obstruction. For the production of this disease two factors seem to be necessary: first, damage and devitalization of the hepatic cells by long-continued dietetic errors, hereditary predisposition or some other cause and second, a slow infection, in most cases with either Bacillus coli or streptococci. In proof of this assertion the author offers the following evidence based on his own experience: (1) animal experiments in which white rats and puppies fed on a diet

high in fat along with intraperitoneal injections of B. coli showed degenerative changes in the hepatic cells, with some increase of fibrous tissue in the hepatic lobules; (2) discovery of either colon bacilli or streptococci in the urine in fourteen of sixteen consecutive cases of infantile cirrhosis of the liver, and (3) cure of the disease in four fairly advanced cases by injections of vaccine when other measures had failed. Some sort of chronic gastro-intestinal disorder was present in all the cases. Gross dietetic errors were noticed in only a small number, but a history of irregular feedings was present in all the cases. Others have reported that the presence of bacilli can be actually demonstrated in the liver in cases of cirrhosis.

GONCE, Madison, Wis.

PARTIAL THORACIC STOMACH WITH SHORT ESOPHAGUS: SEVEN CASES. J. P. MONKHOUSE and S. K. MONTGOMERY, J. LARYNG. & OTOL. **48**:743 (Nov.) 1933.

Monkhouse and Montgomery report seven cases of partially thoracic stomach with short esophagus of mild degree. In six the diagnosis was confirmed by esophagoscopy, and in one it rested on roentgen evidence alone. These cases fall into two groups, those with and those without dysphagia. In both types there is pain which resembles that of the flatulent dyspepsia of cholecystitis. The dysphagia is not steadily progressive as in carcinoma but is intermittent, and for some time, often years, is not severe. It is due to the presence of an ulcerated stricture. Hematemesis may occur in the two groups of cases. The diagnosis rests on roentgen and endoscopic examination. In the former, unless the barium sulphate meal is given in the manner described, the lesion is not seen, and it is essential that the passage of the opaque material should be watched on the screen in order to differentiate the anomaly from a para-esophageal hernia. In cases with dysphagia, esophagoscopy shows a stricture, possibly with visible ulceration, and mucous membrane removed from this level is found to be gastric in character. In the second group no stricture is seen, but a dilatation may be observed at a level which is certainly above the diaphragm and from which gastric mucosa is obtained. Dilation relieves the symptoms in the obstructive type; those without dysphagia receive some benefit from prolonged medical treatment but do not respond well. Owing to the lack of postmortem material many points in the pathologic condition are still obscure.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ADENOMA OF THE PARATHYROID GLANDS ASSOCIATED WITH GENERALIZED OSTEITIS FIBROSA. S. C. DYKE, R. MILNES WALKER and E. FREEMAN, Lancet **2**:530 (Sept. 2) 1933.

"Enough evidence has now accumulated to show that hypercalcaemia with excess excretion of calcium in the urine and signs of skeletal decalcification with formation of cystic spaces in the bones points clearly to the presence of a parathyroid adenoma, and that on careful search the surgeon will seldom be disappointed."

Two cases are reported, both in girls 14 years of age. The first girl showed a serum calcium of 16.7 mg. per hundred cubic centimeters and a total calcium excretion in the urine on an ordinary diet in twenty-four hours of 966 mg. Roentgenograms showed rarefactions of the bones and deformity of the right hip. At operation a soft, oval, maroon-colored tumor (3 by 2 by 1 cm.) was found in the position of the left inferior parathyroid body. The patient stood the operation well and left the hospital much improved, being able to walk with only slight assistance from a stick, whereas on admission she was helplessly crippled. Pain had disappeared completely. After operation the serum calcium dropped to within normal limits in the course of five days.

The second patient was a dwarfed and deformed, intelligent girl. She showed marked genu valgum of both legs, marked curvature of the spine and clubbing of the fingers. Roentgenograms showed a high degree of rarefaction of all the

bones. The serum calcium was 17.7 mg. per hundred cubic centimeters. At operation a dark-colored tumor the size of a walnut was found lying behind the lower pole of the right thyroid lobe. This girl also was much improved following the operation.

LANGMANN, New York.

SERUM TREATMENT OF HODGKIN'S DISEASE. N. R. BARRETT and L. T. BOND, Lancet **2**:855 (Oct. 14) 1933.

Four patients were treated with chicken serum according to the method advocated by Utz and Keatinge. The results were uniformly disappointing.

LANGMANN, New York.

ROENTGENOGRAPHIC SHADOW OF THE DESCENDING AORTA IN CHILDHOOD. J. C. NAVARRO and C. A. HUERGO, Arch. de méd. d. enf. **36**:649 (Nov.) 1933.

In studying the films of the thorax of an infant suffering from asthmatic bronchitis, the authors were struck with the clearly defined shadow of the descending aorta. As there were no lesions of the circulatory apparatus, further observations were made among six hundred roentgenograms available in the pediatric clinic at Buenos Aires. A considerable number showed the descending aorta, and twenty-eight were selected for intensive study. A review of the literature failed to reveal any similar investigation, although interesting reports had been published on the roentgen characteristics of the ascending aorta and of the arch.

In the series of roentgenograms under discussion, practically all represented some form of inflammation of the respiratory apparatus; in no instance, on the other hand, was a lesion of the vascular system demonstrated. The theory is advanced that inflammatory processes of the respiratory tree, recent or remote, restricted or extended, are prone to attack the tunica adventitia of this portion of the artery, rendering it more easily visible. The fact that the aortic shadow is lost at the level of the diaphragm, where contact with the air passages is concluded, is considered significant. A brief abstract of the case histories is attached.

AMESSE, Denver.

GANGLIONEUROMA OF SYMPATHETIC ORIGIN IN A GIRL FIVE YEARS OLD. P. ARMAND-DELILLE, C. LESTOCQUOY and H. GAVOIS, Bull. Soc. de pédiat. de Paris **30**:474 (Oct. 18) 1932.

The child had no symptoms and showed no physical signs of an intrathoracic tumor which was found by roentgenologic examination. It occupied the middle third of the left half of the thorax and extended to the posterior mediastinum. An artificial pneumothorax was performed and by further roentgenologic study it was learned that the lung was free and not involved in the neoplasm. The neoplasm was removed and found to be about the size of a coconut. Histologically it had the structure of a ganglioneuroma.

BENJAMIN, Montreal, Canada.

INTERMITTENT SWELLING AT THE BASE OF THE NECK OCCURRING DURING EXERTION IN A GIRL FIVE YEARS OLD. DISCUSSION OF DIAGNOSIS. H. JANET and S. HUGUET, Bull. Soc. de pédiat. de Paris **30**:480 (Oct. 18) 1932.

A healthy girl, 5 years old, presented a swelling at the base of the neck only when she exerted herself, thus apparently rigidly fixing the diaphragm. It was noticed first at the age of 3 years, when she would shout. The authors do not think that the swelling is due to a condition in the thyroid or the thymus gland, nor is it associated with the trachea. They think that it may possibly be due to a mass of fatty and areolar tissue which is subject to pressure as a result of venous congestion of the great vessels at the base of the neck. Those discussing the

case believe that it is only a marked accentuation of that which occurs normally and that this accentuation is due to a weakness of the tissues covering the superior outlet of the thoracic cage. There is a photograph of the child taken while the swelling showed plainly.

BENJAMIN, Montreal, Canada.

PULMONARY AND MEDULLARY TUMORS (PROBABLY SARCOMA) IN AN INFANT ONE YEAR OLD. SUCCESSFUL ROENTGEN TREATMENT. B. WEILL-HALLÉ, CLAIRE VOGT, DUHEM and DUBOST, Bull. Soc. de pédiat. de Paris **30**:513 (Oct. 18) 1932.

A boy, a year old, presented paraplegia which developed at the age of 10 months. Physical examination revealed bulging of the lower two thirds of the left side of the chest, and over this area the percussion note was flat and breath sounds could not be heard; these were the only abnormal findings in addition to the paraplegia. Roentgenologic examination showed a dense shadow which occupied the lower two thirds of the left side of the thorax and the mediastinum; the spinal column was normal. Lumbar puncture yielded a xanthochromic fluid. clear fluid was obtained on cisternal puncture, and iodized poppy-seed oil 40 per cent was injected. This demonstrated a block at the twelfth dorsal vertebra. Roentgen therapy was given and was followed by an almost complete disappearance of the tumor as well as some improvement in the nervous symptoms and signs in about two months. This is believed to be only temporary, as occurs not infrequently in cases of extensive sarcoma. In this case the authors make a diagnosis of sarcoma of the left lung with extradural metastasis which produced paraplegia by pressure on the spinal cord. It is noteworthy that no respiratory symptoms were present.

BENJAMIN, Montreal, Canada.

TWO INSTANCES OF SAFETY-PINS REMAINING FOR MONTHS IN THE SMALL INTESTINE. HENRARD, J. de radiol. et d'électrol. **17**:320 (June) 1933.

A girl, aged 5 months, swallowed an open safety-pin which was seen in the stomach a few hours later, in the lower duodenum after sixty-three hours, in the jejunum on the fourth day, and in the lower portion of the small intestine on the ninth day, where it still appeared two months and twenty-three days after ingestion, lying across the ileocecal valve with its point in the small intestine. Eight months after the accident, the position of the pin being unchanged, operation was accepted and successfully performed.

A girl, aged 8 months, swallowed an open safety-pin and a coin; the latter passed the rectum spontaneously the next day. After the pin in the lower intestine had remained for four months it was also evacuated.

VINTON, Brooklyn.

TRANSFUSION FOR MELENA. E. BANSSILLON, Nourrisson **21**:236 (July) 1933.

After severe hematemesis and melena, a baby, badly exsanguinated on the third postnatal day, was revived by a direct transfusion from the father into a vein at the elbow. This is advised in preference to a transfusion into the superior longitudinal sinus.

MCCLELLAND, Cleveland.

PYLORIC STENOSIS IN INFANCY. GASTON LYON and ANDRÉ BERGERET, Presse méd. **41**:1665 (Oct. 28) 1933.

In a discussion of hypertrophic pyloric stenosis, Lyon and Bergeret call attention to the fact that it may occur in the adult, citing the recent case of Harvier and Brun (*Paris méd.* **1**:173, 1933) in a woman 60 years of age, and a number of others previously reported. Various descriptive terms have been applied to the condition as found in the adult, such as "hypertrophic sclerosis," fibroid of

the pylorus" and "simple hypertrophy of the pylorus." It has been frequently confused with linitis plastica. Whether it is always congenital is disputed. It has been observed in cases of ulcer. In favor of its being congenital is the frequency of a history of gastric disturbances suffered since childhood.

In infants, the diagnosis is fairly simple, therapeutic tests serving to exclude spasm which is the only condition presenting a serious differential problem. In adults, the symptoms may be vague and a malignant process may be suspected, or the diagnosis may be made only at autopsy.

Two cases of infantile pyloric stenosis are reported, with uneventful recovery following surgical intervention.

BIEKER, St. Petersburg, Fla.

TREATMENT OF COLLAPSE IN THE COURSE OF DIABETIC COMA. M. LABBÉ and R. BOULIN, Presse méd. **41**:1705 (Nov. 4) 1933.

Labbé and Boulin find the slow injection of epinephrine intravenously invaluable in the treatment of cardiac collapse in the course of diabetic coma. They give 1 mg. diluted in about a liter of physiologic solution of sodium chloride. The lowering of the blood pressure presaging collapse may be controlled by intramuscular injections of epinephrine, or by ephedrine given orally, but if collapse occurs, intramuscular injections are ineffective. If the pressure falls after the intravenous injection, the treatment should be repeated. For a few days following, epinephrine should be administered intramuscularly or ephedrine orally four times a day.

BIEKER, St. Petersburg, Fla.

DIABETES IN INFANCY. P. LEREBOULLET, Progrès méd., Oct. 21, 1933, p. 1760.

Diabetes in children is unusual but not uncommon. Lereboullet has observed over 100 cases in children under 10 years of age. He observed one case in an infant 3 weeks of age and others in children 3, 5 and 7 months of age. Etiologically there is probably a strong familial tendency, with an acute infection as the incitant. Certain other conditions, such as congenital syphilis, typhoid fever and cranial injuries, have been noted as factors. The most frequent signs are polydipsia, polyuria, polyphagia (there may be anorexia) and hepatomegalia. The condition exists in four forms: (1) lowered tolerance for carbohydrate with tendencies to acidosis and malnutrition; (2) lowered tolerance but no malnutrition; (3) a form amenable to treatment with insulin and of steady tolerance, and (4) a form in which intolerance is shown only occasionally. With modern therapy, the prognosis is not hopeless. The treatment consists in finding the proper carbohydrate balance and in keeping this at a stage for proper nutrition by the administration of insulin.

SANFORD, Chicago.

IMPORTANCE OF THE BLOOD GROUPS. R. TURPIN and A. CARATZALI, Rev. franç. de puéricult. **1**:86 (May) 1933.

From the evidence available it may be concluded that the blood group is a hereditary characteristic, that it is inherent in the constitution of the individual, that it may serve as a base for an ethno-anthropologic classification and that it appears to be associated with certain normal and perhaps with pathologic hereditary characteristics.

CRANE, Chicago.

ERYTHREMIA: FORM OF VON JAKSCH-LUZET DISEASE. B. VASILE, Pediatria **41**:1412 (Nov. 1) 1933.

In a case of von Jaksch-Luzet disease the hermatologic picture represented a pure and extreme myelocytosis.

SIGNORELLI, New Orleans.

A Case of Pyopneumothorax. Giovanni Frollo, Pediatria **41**:1418 (Nov.) 1933.

Frollo directs attention to certain roentgen features which, studied in relation to the observations at autopsy, might lead to a better understanding of the possible alterations to be met in spontaneous pneumothorax.

Signorelli, New Orleans.

Accidents in Infancy Caused by Insulin. A. de Rezende, Arch. de pediat. d. Rio de Janeiro **5**:353 (Aug.) 1933.

Children who are dystrophic should have a smaller dosage of insulin than that calculated for normal weight. All of the accidents that de Rezende has observed have been in cases in which an increased dosage was given. The most common accidents are vomiting, hypothermia and convulsions. Also, in cases in which there is a tendency to diarrhea the insulin should be given on alternate days or even at intervals of three days.

Sanford, Chicago.

Urinary Stone in a Child. J. M. da Rocha and I. V. Lima, Arch. de pediat. de Rio de Janeiro **5**:357 (Aug.) 1933.

A boy, 8 years old, had complained of painful urination for two years. The urine showed traces of blood, albumin and cells. The stone was seen by roentgenogram and was easily removed by subpubic incision under ethylene anesthesia.

Sanford, Chicago.

Mixed Infections. H. Schlossberger and J. Grillo, Paidoterapia **12**:141 (June) 1933.

Three different types of mixed infections can be distinguished. In the first, the primary infection is aggravated by the secondary infection; in the second, the two develop independently of each other, and in the third, one influences the other in such a way that either improvement or complete recovery results.

The influence of one infection on another cannot be attributed to the action of one organism on another, but probably results from the action of one organism on the body increasing the latter's resistance against the other organism. That an improvement is not due to antagonism of the two infections is suggested by the fact that many chemical substances influence the course of the disease in the same way as an accidental secondary infection.

In the cases in which a patient with an infectious disease is improved or cured as a result of a secondary infection the improvement or cure is probably due to a modification of the whole metabolic structure as a result of the mixed infection.

Herron, Spokane, Wash.

Rare Abdominal Diseases in Infancy. Heinrich Fleischer, Arch. f. Kinderh. **100**:80 (Sept. 29) 1933.

An infant, 2 weeks old, presented chylous ascites and scleredema. Keratomalacia appeared before the infant died. Autopsy failed to reveal any cause for the ascites. An infant, 5 months old, had pneumococcic peritonitis of twenty-four days' duration before generalized sepsis and pneumococcic meningitis caused death. Abdominal paracentesis during life revealed pneumococci in the purulent fluid.

LeMaster, Evanston, Ill.

A Case of Generalized Granulomatous Xanthomatosis (Schüller-Christian Disease). F. v. Bernuth, Arch. f. Kinderh. **100**:115 (Sept. 29) 1933.

Schüller-Christian disease was observed in a boy 3½ years old. At first examination, excessive thirst and numerous small reddish-brown cutaneous nodules were the only signs. Later the roentgenograms showed rarefied areas in the bones of the skull and pelvis. Biopsy of a cutaneous nodule showed foam cells and giant cells. There was no exophthalmos. After observation for several months no change was noted except an increase in the number of tumors in the skin.

LeMaster, Evanston, Ill.

Sugar Therapy in Nephritis. Zoltán von Bókay and Ladislaus von Kostyál, Arch. f. Kinderh. **100**:123 (Sept. 29) 1933.

Unusually good results are reported in fifty children with nephritis who were treated by the sugar diet. Thirty-four of the children had acute hemorrhagic glomerulitis; four, subacute hemorrhagic nephritis; five, chronic nephritis; six, nephrosis, and one, erysipelas and sepsis complicating a postscarlatinal nephritis. The diet consisted of from 250 to 400 Gm. of malt or potato sugar with water restricted as much as the child could tolerate. After definite improvement began, fruits were added to the diet. If uremia or vomiting occurred, from 10 to 20 per cent dextrose solution and calcium salts were injected intravenously. Several case histories are presented in detail. The authors suggest ways in which the sugar diet may favorably influence metabolic processes during the course of nephritis.

LeMaster, Evanston, Ill.

Physiologicochemical Investigations in Chylous Ascites. Wilhelm Hertz, Arch. f. Kinderh. **100**:193 (Oct. 31) 1933.

Hertz made complete chemical analyses of the ascitic fluid from an infant with chylous ascites and scleredema. Various theories concerning the etiology of scleredema are discussed.

LeMaster, Evanston, Ill.

Criticism of So-Called Parathyroid Extract Eosinophilia with Remarks on the Influence of the Intake of Nourishment on the Blood Eosinophilia. Heinrich Fleischer, Arch. f. Kinderh. **100**:220 (Oct.) 1933.

In a previous publication, Lenart and Lederer reported that from four to five hours after an injection of parathyroid extract into certain type fasting children the eosinophil count decreased at least 30 per cent in normal children, increased at least 30 per cent in children with diphtheria or chorea and showed a plus or minus variation of less than 20 per cent in children with true epilepsy. Repeating these tests, Fleischer was unable to confirm the results obtained by Lenart and Lederer. He could demonstrate no effect on the eosinophil count by injecting parathyroid extract. In some of the cases, after a feeding the eosinophil count was increased. This was interpreted as possibly being due to a reaction to foreign protein.

LeMaster, Evanston, Ill.

Cardiospasm in Childhood. Hansen, Beitr. z. klin. Chir. **157**:617, 1933.

A 7 year old girl had a history of vomiting of undigested food, with gradual progressive weakness.

A series of roentgenograms showed barium sulphate passing through the esophagus, but there was definite stenosis present on entering the stomach. After one and one-half hours stasis was still present in the lower third of the esophagus.

Operation revealed scarred changes on the under surface of the diaphragm, and anastomosis of the esophagus with the anterior wall of the stomach was performed. Improvement was evident soon after the operation and was marked even after eight months.

RUBIN, Boston.

ARTHROPNEUMOROENTGENOGRAPHY. J. OBERBOLZER, Beitr. z. klin. Chir. **158**: 113, 1933.

This article is a complete and detailed account of the technic of arthropneumoroentgenography. The appearance of a normal knee following this method is shown in detail. There is also a complete description of certain pathologic conditions of the knee joints following this technic. The author emphasizes the fact that this is a method without danger and has been carried out on older children without any mishap or discomfort.

This method gives a clear understanding and picture of the normal knee joint. It also allows one to determine the amount of damage done to the meniscus, crucial ligaments, lateral ligaments and capsules. The diagnosis of osteochondritis dissecans is insured with this technic.

Further work on other joints must be done before comparably good results will be obtained.

RUBIN, Boston.

NONTUBERCULOUS DISEASE OF PSOAS MUSCLE IN CHILDHOOD. FRIEDRICH KLAGES, Beitr. z. klin. Chir. **158**:171, 1933.

The author states that this condition is not uncommon. It may be secondary, such as infection of the psoas muscle following trauma or the presence of a foreign body, or due to a pathologic condition in neighboring organs—appendicitis, nephritis or osteomyelitis. There is also primary psoitis, which should be conservatively treated in mild cases and surgically treated in more severe cases with abscess formation.

RUBIN, Boston.

GALACTOSURIA IN A BOY WITH NEUROFIBROMATOSIS. G. FANCONI, Jahrb. f. Kinderh. **138**:1 (Jan.) 1933.

A poorly developed boy, aged 9 years, with familial neurofibromatosis and zonular cataract was accidentally found to excrete galactose whenever he ingested milk, lactose or galactose. After small doses of galactose (2 Gm.), he excreted 1 Gm.; after large doses (6 Gm.), he excreted 5.2 Gm. The larger doses caused a rise of sugar in the blood to 466 mg. per hundred cubic centimeters and symptoms of apathy and weakness.

CLAUSEN, Rochester, N. Y.

PATHOGENESIS OF ENURESIS. S. EDERER and E. VON LEDERER, Jahrb. f. Kinderh. **138**:21 (Jan.) 1933.

Evidence is presented to show that the normal control of the sphincter of the bladder both during the waking state and during sleep is an acquired (conditioned) reflex. It is shown that many persons with enuresis, although intelligent, may have a specific defect such as faulty deep sensation, as tested objectively; it is assumed that they may have weak "organ-feeling." A treatment successful in 80 per cent of cases is based on the effort to condition the bladder-reflex properly: 1. The child is wakened at the same time each night; he must be fully awake and conscious of keeping the bladder closed before urination. 2. An effort is made to teach the child to awake by himself. This is brought about by talking to him and by the use of ephedrine (from 25 to 50 mg.). 3. The child is carefully and continuously supervised.

CLAUSEN, Rochester, N. Y

SHELL-SHAPED PROLIFERATIONS OF THE ENTIRE UVEAL TRACT WITH INVOLVEMENT OF THE ORBIT: A CLINICAL CONTRIBUTION ON ALEUKEMIC LYMPHADENOSIS AND LYMPHOSARCOMATOSIS OF THE EYE; REPORT OF TWO CASES. G. B. BIETTI, Klin. Monatsbl. f. Augenh. **90**:308 (March) 1933.

A child, aged 3 months, showed extensively swollen glands of the left side of the neck and occiput and enlargement of the liver and spleen. A whitish-yellow mass, adjacent to Descemet's membrane, covered nearly the whole iris of the left eye. The intra-ocular tension was increased. Histologic examination revealed infiltration of the choroid with round cells, larger than lymphocytes and resembling lymphoblasts. The mass in the anterior chamber was an exudate consisting chiefly of decayed infiltration cells. Similarly infiltrated zones were found around the posterior ciliary nerves and vessels, extending into the orbit, and near the sclera in the orbital tissue.

A man, aged 48, presented extensive edema of the lids of the left eye, extending almost to the ear. This swelling developed within a year after the patient had discovered a small red spot in the conjunctiva. The orbit was exenterated, and masses extending into the nasal cavities were found, which had eroded the bone. Several types of cells, especially lymphoblasts, dwarf cells and large cells with a very large nucleus, were found histologically. No metastases were noted at the time of the operation, but resection of the angle of the jaw became necessary, and death from involvement of the liver occurred four months later. A combination of undoubted symptoms of sarcoma and aleukemic lymphoma prompted Bietti to consider the condition in this case as a combination of these two diseases.

STOLL, Cincinnati [ARCH. OPHTH.]

TREATMENT OF ADHESIVE RHEUMATIC PERICARDITIS. H. W. PÄSSLER, München. med. Wchnschr. **80**:1247 (Aug. 11) 1933.

Pässler discusses the results in patients who had a resection of the pericardium for adhesive pericarditis. A total of seventy-three operations were performed by thirty-three surgeons. Nineteen pericardectomies were performed at the Frankfort Klinik. Owing to technical difficulties the immediate operative mortality was high. Many patients were greatly improved. However, among those who were improved, many a few years later were either incapacitated or dead. The patients did not have a recurrence of adhesive pericarditis, but suffered from other rheumatic manifestations such as angina, pleurisy, polyarthritis, endocarditis and myocarditis. Successful treatment of the pericarditis had no effect on the progress of the rheumatism in other parts of the body. This emphasizes the importance of treating the underlying disease by tonsillectomy, or whatever is deemed necessary, in order to prolong the beneficial effects of the pericardectomy. The heart should be freed of adhesions as much as possible.

BRAHDY, Mount Vernon, N. Y.

CHANGES IN THE CENTRAL NERVOUS SYSTEM IN GENERALIZED XANTHOMATOSIS OF THE CHRISTIAN-SCHÜLLER TYPE. H. CHIARI, Virchows Arch. f. path. Anat. **288**:527, 1933.

In cases of generalized xanthomatosis, lipoid infiltration of the infundibular region has been found with comparative frequency, whereas xanthomatous changes of the other parts of the central nervous system are extremely rare. The patient whose brain was thoroughly examined by Chiari suffered from generalized xanthomatosis and tuberculosis of the lungs, to which he succumbed. The patient had symptoms of diabetes insipidus, headaches, double vision, disturbance of mastication and hearing and symptoms suggesting a tumor of the cerebellopontile region. In addition, typical xanthomatous changes of the bones were found by roentgenogram and confirmed at autopsy. The unusual changes, however, were found in the central nervous system. Macroscopically, the pia mater showed small yellow nodules in the region of the lobulus semilunaris inferior of the cerebellum. At the base of the brain, the tuber cinereum protruded markedly and the infundibulum

was greatly enlarged; both were pale gray. Yellow nodes of different sizes consisting of cells containing lipoids were found in the right frontal lobe, in the corpus callosum and in both occipital lobes. The most remarkable infiltrations were those found in the cerebellum and the pedunculi pontis ad cerebellum. Several nodules were seen in the upper part of the cervical region of the spinal cord. The basal nuclei and the cortex of the brain were entirely free from infiltration.

Histologically, the lesions in the bones and dura mater showed a granulation tissue containing numerous lymphocytes which included smaller and larger foam cells containing doubly refractive substances. Similar composition of the tissue was found in the brain lesions, which contained more or less connective tissue, depending on the age of the lesions. It is of special interest that, whereas the anterior lobe of the pituitary gland was free from the infiltration, the posterior lobe, the stalk of the hypophysis, the infundibulum and the tuber cinereum contained connective tissue densely filled with lymphocytes; in the latter region no solid infiltration of the tissue was found, but the walls of the blood vessels were enclosed by a coat of foam cells and a few lymphocytes.

The changes so far described involved the white substance of the brain which was actually involved in the xanthomatous process. In parts of the central nervous system located far from these lesions, only slight changes were found, consisting of depositions of sudanophil granules in the *Deckzellen* of the small arteries at many places. The ganglion cells of the cerebrum showed no changes. The ganglion cells of the anterior horn of the spinal cord in the neighborhood of the lesion described earlier showed a few small sudanophils, but no doubly refractive granules. The myelin sheaths in the large xanthomatous lesions were destroyed and those in the surrounding tissue showed evidence of swelling and destruction. This was true also for the neurofibrils and, to a certain degree, for the glia fibers, though the latter seemed to be less involved.

Chiari tried to establish the origin of the foam cells by a stain which is a modification of Penfield and Rydberg's stain. It appears evident, from previous observations, that the foam cells of the large xanthomatous foci are of mesenchymal origin. With this method, Chiari was able to show that the isolated foam cells or *grobluеckigen* cells are probably derived from oligodendrogia and microglia cells, which were greatly changed by the deposition of lipoid substance. He is inclined to believe that the oligodendroglia cells and the Hortega cells take an active part in the accumulation of lipoid substance. Whether their activity precedes, however, the deposition of lipoid substance in the mesenchymal cells cannot be determined finally on the basis of his study.

SCHOENTHAL, New York.

APPEARANCE OF A CEPHALHEMATOMA IN A CHILD AGED SEVENTEEN MONTHS. A. J. CHURA, Bratisl. lekár. listy **13**:206 (May) 1933.

Chura reports a case of cephalhematoma in a child at the age of 17 months, the condition being difficult to diagnose on account of the age. The etiology was indefinite, but because of the tendency to a constitutional disposition it appeared that a blow tangent to the surface of the cranium was probably the principal causative influence. Expectant treatment was indicated so long as the tumor did not give evidence of suppuration.

VINTON, Brooklyn.

ANEMIA OF CHILDHOOD. M. S. LAPTER-POPOV, Pediatriya **14**:483, 1931.

Although many authors define anemia as a decrease in the amount of hemoglobin and erythrocytes and a decrease in the total quantity of blood, the classification of the several forms of anemia remains debatable. In the analysis of his material Lapter-Popov adopted the classification of Marfan. Marfan, basing his conclusions on clinical observations, classified anemias of childhood as follows: (1) simple anemia caused by autointoxication and intoxication resulting from

infectious diseases; (2) pseudoleukemic anemia with splenomegaly and (3) anemia caused by a shortage of iron and chlorosis of early childhood. The last form occurs frequently.

The causes of anemia may be loss of blood, infectious diseases, swellings, constitutional defects, failure in correlation of the organs of internal secretion, insufficient and inadequate diet, poor living conditions and chronic poisoning. In view of the fact that erythrocytes live from thirty to forty days and that from one tenth to one thirtieth of the total amount perish every day, an equal amount must be recreated. Any imbalance caused by the diminution in the number or an increased need of new blood cells causes anemia.

Anemia of childhood occurs frequently and has characteristics rarely observed in anemia at maturity, even in its severe manifestations. Simultaneously with erythrocytes invariably occur many white blood cells, i. e., myelocytes, in the majority of cases neutrophilic. The percentage of erythrocytes is greater than in mature people. The leukocyte content also has a specific character; leukocytes are present in a greater number, and among them are present more lymphocytes, than at a greater age. This profusion of cells of the lymphoid order lasts up to the fifth year, then decreases until the leukocyte content approaches that found at maturity. The hemoglobin content in each separate erythrocyte is somewhat less than in grown persons, and the color index is less than at majority, which explains the fact that anemia of childhood is of a hypochromic character. One of the frequent causes of the hypochromic forms of anemia is a diet of goat's milk. In general it may be stated that anemia of childhood depends on a variety of causes and occurs frequently.

The material under discussion consists of fifty cases of anemia observed during a period of five years in the Ormsk Medical Institute. Twelve cases are particularly interesting and, following Marfan, are classified as follows: (1) simple severe forms of anemia, five cases; (2) pseudoleukemic anemia with enlargement of the spleen, four cases; (3) anemia of the chlorotic type, one case; (4) anemia due to lead poisoning, one case.

Simple anemia at an early age is characterized by a decrease of hemoglobin and erythrocytes. In more severe cases poikilocytosis and polychromatosis are to be noted. In very young children normoblasts are to be observed; the number of leukocytes usually increases slightly at the expense of the lymphocytes and monocytes. One of the characteristics of simple anemia in children is the combination with symptoms of rickets. The duration of the disease, if prolonged, depends on the basic cause, which may be inherited syphilis, incorrect diet, indigestion or loss of blood. The treatment consists in administering preparations of iron and, rarely, arsenic.

Pseudoleukemic anemia is characterized by considerable decrease of the erythrocytes and hemoglobin, leukocytosis and lymphocytosis, the presence of grain-containing erythrocytes, the frequent presence of various myelocytes in the blood and enlargement of the spleen and liver.

Chlorosis in breast-fed infants is due to a shortage of iron and is characterized by a considerable decrease of hemoglobin with a normal number of erythrocytes, low color index, absence of leukocytosis and absence of erythroblasts and myelocytes. This form of anemia is particularly frequent in twins when the total iron supplied by the mother has been insufficient for both children.

In conclusion it may be said that anemia is more frequent in childhood than in any other period. It is interesting to note that in very young children with anemia there are elements in the blood which are also present during the prenatal stages. The more severe the anemia and the younger the patient the greater is the number of such elements. Pernicious anemia is rare, but aplastic anemia is frequent. Anemias are especially frequent after infectious diseases (malaria) and in combination with rickets or inherited syphilis. YAMPOLSKY, Atlanta, Ga.

GENERALIZED XANTHOMATOSIS. O. K. SVENNINGSEN, Acta radiol. **14**:491 (Oct.) 1933.

This rare disease figures under the name of Christian's syndrome. It consists of a triad made up of the symptoms of diabetes insipidus, exophthalmos and defects in the cranial bones. It is characterized by the presence of xanthoma cells in the defects and in patches and nodules. "A xanthoma cell is a large connective tissue cell whose plasma, besides containing one or several nuclei, has become vacuolized and contains numerous granules that stain black with osmic acid. In certain forms of the disease these cells occur diffusely distributed through the various tissues of the body, in which case the condition is termed xanthomatosis." Rowland describes five groups: (1) xanthoma palpebrarum and multiplex xanthoma; (2) xanthomyeloma in the sheaths of tendons; (3) visceral and generalized xanthoma, including Christian's syndrome; (4) Niemann-Pick disease; (5) xanthoma diabeticorum. The initial symptoms vary enormously. They appear between the first and the seventh year of life. In by far the greater number of cases gingivitis and loose teeth are the first manifestations. In some, exophthalmos, polyuria and polydipsia are the earliest indications. Beside these, some of the most frequently mentioned symptoms are strabismus, arrested growth, deafness, otorrhea, pains in the head and back, xanthomatous eruptions of the skin, adiposogenital dystrophy, infantilism, hydrocephalus, yellow spots on the retina, neuritis of the optic nerve, tumors of the neck, pelvis and liver, icterus, difficult walk, changes in the hematic picture and hypercholesteremia. The intellectual faculties do not become impaired, and the Pirquet and Wassermann reactions are always negative. The author details a long and full account of a case.

VINTON, Brooklyn.

HYPERTENSION IN A YOUNG CHILD. A. F. A. S. WESTRIENEN, Maandschr. v. kindergeneesk. **3**:156 (Jan.) 1934.

A case of severe hypertension in a girl, aged 8 years, is reported, and suggestions for the explanation of this condition are discussed.

VAN CREVELD, Amsterdam, The Netherlands.

DIAGNOSTIC DIFFICULTIES IN CASES OF FOREIGN BODIES IN THE LOWER RESPIRATORY PASSAGES. A. DE KLEYN and C. R. J. VERSTEEGH, Maandschr. v. kindergeneesk. **3**:183 (Feb.) 1934.

Stress is laid on an exact history and examination and roentgenograms taken during inspiration and expiration. A case is reported of a child aged 2 years in whom a metal medal, after having perforated the trachea, was found in the esophagus, and another case is reported of a child aged 14 months whose roentgenograms showed a shadow which gave the impression of a foreign body, but which finally proved to be caused by the ossification nucleus of the manubrium sterni.

VAN CREVELD, Amsterdam, The Netherlands.

GLYCOGEN DISEASE. S. VAN CREVELD, Nederl. tijdschr. v. geneesk. **77**:4659 (Oct. 14) 1933.

Some years ago the author described a number of investigations carried out on a boy who had had a large liver since birth, who clinically gave the impression of adiposogenital dystrophia, and who, in addition, showed a peculiar and until then unknown disturbance in carbohydrate metabolism. This disturbance was regarded as resulting from an accumulation of glycogen, especially in the liver, which could be mobilized only with difficulty. The condition was regarded as hepatomegalia glycogenica and has since been described from a pathologic point of view. The interest in this disease has greatly increased. In this article further investigations carried out on the boy and those carried out on a second patient (a girl) with hepatomegalia glycogenica are extensively described. The glycogen metabolism in both patients was studied, and the differential diagnosis was made from other

chronic diseases of the liver. A method of determining the glycogen content in 1 cc. of blood is described. The results of the chemical investigation of the organs of a baby with idiopathic hypertrophia of the heart caused by the accumulation of glycogen are reported.

AUTHOR'S ABSTRACT.

OSTEOCHONDRITIS DEFORMANS JUVENILIS OF THE LOWER END OF THE HUMERUS. J. F. HAGEN and P. BISSCHOP, Nederl. tijdschr. v. geneesk. **77**:4977 (Nov. 4) 1933.

The author describes a case of this disease in a boy, aged 8 years.

VAN CREVELD, Amsterdam, The Netherlands.

CONGENITAL SHORT ESOPHAGUS WITH ULCUS PEPTICUM ESOPHAGI. I. L. HAROEN and P. G. GERLINGS, Nederl. tijdschr. v. geneesk. **78**:655 (Feb. 10) 1934.

A case of congenital short esophagus with peptic ulcer of the esophagus in a girl, aged 3 years, is reported. The patient had vomited since birth and had frequent hematemesis and melena and severe anemia. A roentgenogram is shown.

VAN CREVELD, Amsterdam, The Netherlands.

THE ARA-TAKATA TEST IN CIRRHOSIS OF THE LIVER. J. H. R. VAN GINKEL, Nederl. tijdschr. v. geneesk. **78**:991 (March 3) 1934.

The Ara-Takata colloidal test, as modified by Jezler, and its application in the diagnosis of hepatic diseases, are described. The principle of the method is indicated, as well as the technic, which has been more or less simplified by the author. The precipitation is due to an increase of the globulin fraction in the serum. The author's results are compared with the data of Jezler and Rohrer. The statement that in nonhepatic diseases the reaction should always be negative has not been borne out. The Ara-Takata test is useful in the differential diagnosis in which cirrhosis of the liver and other hepatic diseases in an advanced stage are considered, and in several cases the reaction has proved to be of clinical value.

VAN CREVELD, Amsterdam, The Netherlands.

PATHOGENESIS OF ASTHMA. P. DE BERSAQUES and A. BERAT, Nederl. tijdschr. v. geneesk. **78**:1728 (April 21) 1934.

The three fundamental factors which are necessary for the causation of asthma are: disturbance of the endocrine function of the liver, lability of the nervous system and a lesion of the respiratory system. Hypersensitivity to some allergens and other endocrine disturbances may act as additional factors.

VAN CREVELD, Amsterdam, The Netherlands.

STRUMA IN CHILDREN IN HOLIDAY-COLONIES. A. A. KOOPAL, Tijdschr. v. soc. geneesk. (Holland) **11**:195 (Oct.) 1933.

Between the last part of 1932 and July 1933, the author examined for goiter a large number of children from all parts of Holland during their stay in holiday colonies. It appeared that of 1,502 boys 16.5 per cent had struma, and of 1,509 girls, 28.3 per cent; the average percentage was 23. The percentage of cases of struma increases with age. The regions from which the children came could be divided into regions with much struma and those without struma. In comparing the figures of the frequency of struma and the iodine content of the water in different regions of Holland, a confirmation of the theory of iodine deficiency could in general be given. Struma has no direct influence on the sending of the children to the holiday colonies, and during their stay there the children with struma did not show definite symptoms of illness.

VAN CREVELD, Amsterdam, The Netherlands.

Nervous Diseases

A Histological Study of the Adrenal Cortex in Mongolism. L. C. Hirning and S. Farher, Am. J. Path. **10**:435 (May) 1934.

The suprarenal glands do not show any characteristic morphologic change in mongolian idiocy. However, with a method for measurement of the thickness of the cortex, it was shown in fifteen cases that there is definite hypoplasia of the cortex, which becomes more conspicuous as maturity advances.

Moore, New York.

The Rôle of Masturbation Conflict in the Development of Psycho-Neurotic Symptoms. Baruch Silverman, Canad. M. A. J. **30**:287 (March) 1934.

The author reports six cases illustrative of the effect of the mental conflict accompanying the habit or the complete cessation of the habit of masturbation. Following a careful study of a large number of such patients his conclusions were:

1. Masturbation per se does no definite harm and does not result in psychoneurotic or psychotic symptoms, except when it is excessive.
2. Only when this habit is present in shy, sensitive, introverted persons and is accompanied by conflict do symptoms develop.
3. The use of phantasy in masturbation strengthens the tendency to avoid reality in any difficult situation.
4. When there is complete cessation of the habit following conflict a critical situation is created which may easily result in the development of psychoneurotic symptoms.

Moore, Omaha.

A Measure of Delinquency. A. R. Gilliland and J. C. Eberhart, J. Crim. Law & Criminol. **24**:736 (Nov.-Dec.) 1933.

This paper is a report of the application of H. R. Laslett's word association test for delinquency, which was given to 546 Chicago boys who were selected so as to represent widely varied social gradations. The primary value of such a test is in the prevention of delinquency. Laslett's results indicated that this technic may be expected to pick out potential delinquents from an unselected group. Results from the application of the test to the Chicago boys, however, did not confirm this prediction, and the question of the relative influences of social delinquency and of social and economic levels on the scores obtained with the association test remains unanswered.

Selling, Joliet, Ill. [Arch. Neurol. & Psychiat.]

Thorotrast Encephalography by Cisterna Puncture. F. O. Coe, L. S. Otell and O. F. Hedley, M. Ann. District of Columbia **2**:277 (Dec.) 1933.

The authors present a preliminary report of experimental studies with the subarachnoid injection of thorium dioxide (thorotrast). The studies resulted from a search for a substance that would most closely conform to the requirements of an ideal agent for visualizing the cerebral ventricles and the subarachnoid spaces. Such an agent should be nontoxic and nonirritating, should cast a dense shadow, should be miscible with the cerebrospinal fluid and should be readily eliminated. Four monkeys were used. Two cubic centimeters of fluid was withdrawn from the cisterna, and 6 cc. of thorium dioxide injected. This was done under the fluoroscope. The thorium dioxide was observed to pass downward and upward as a diffuse opacity. The cerebral sulci, as well as the ventricles, were clearly outlined. Roentgenograms taken after thirty minutes showed even better visualization. Three of the monkeys died within twenty-four hours, and the fourth was killed. In a series of five monkeys 2 cc. of thorium dioxide was injected. The roentgenograms were practically as satisfactory as those for the first series. However, only one of the animals showed no ill effects; the others presented slight or severe hemi-

plegia. Roentgenograms taken after a week showed much of the thorium dioxide gone; at the end of four months only a slight residue was detected. The authors are enthusiastic over the roentgenographic results, but they think that the method is still too hazardous to warrant its use as a clinical procedure.

SCHNEIDER, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.]

A NEW FORM OF MEDULLOBLASTOMA—MEDULLOMYOBLASTOMA. G. MARINESCO and M. GOLDSTEIN, Ann. d'anat. path. **10**:513, 1933.

In a girl 5 years old a tumor of the vermis of the cerebellum of an unusual character was found at autopsy. In general, the tumor had the histologic character of a medulloblastoma. In addition there was a large admixture of striated muscle fibers. These were found in various stages of embryonic development, up to fully differentiated muscle fibers. In a discussion of the histogenesis no definite conclusions are arrived at, except that an embryonic factor in the development of the tumor is apparent.

MELNICK, Chicago. [ARCH. PATH.]

PARALYSIS OF THE LEFT ARM FOLLOWING CARBON MONOXIDE POISONING. JEAN HALLÉ and JACQUES ODINET, Bull. Soc. de pédiat. de Paris **30**:157 (March 15) 1932.

A boy, 3 years old, was one of a family all the members of which were subjected to the fumes which emanated from a poorly set up stove which was lighted for the first time one cold winter night. The child was discovered in a coma after he had been in this atmosphere for about twenty hours. His head was found to be caught between two bars of his crib, one of which was pressing on his left clavicle and the other on the right side of his neck. He was dyspneic and cyanosed, and when he was revived it was noticed that he had left brachial plexus paralysis. It is believed that the latter was caused by carbon monoxide poisoning, although the compression of the right clavicular region is considered as a possible etiologic factor.

BENJAMIN, Montreal, Canada.

MENINGITIS DUE TO PFEIFFER'S BACILLUS IN AN INFANT; CURE. G. PAISSEAU, P. TORNANT and G. PATEY, Bull. Soc. de pédiat. de Paris **31**:93 (Feb. 21) 1933.

A girl, 10 months old, had an inflammatory swelling of the right elbow, which was incised. Soon after, convulsions developed. There were no frank signs of meningitis, but lumbar puncture yielded a purulent fluid which contained Pfeiffer's bacilli. Intrathecal injections of antimeningococcic serum were given until a bacteriologic report of the growth of Bacillus influenzae was obtained; thereafter a number of intraspinal and cisternal injections of an acridine dye were administered, followed by a number of similar injections of a colloidal silver preparation. The infant improved, but a relapse occurred after a short interval. She was again given intrathecal injections of an acridine dye, followed by colloidal silver. She recovered, but it is noteworthy that about two and a half months after the onset of the meninigitis, when her condition seemed normal except for some apparent nervous sequelae, the spinal fluid still showed 100 lymphocytes per cubic millimeter. When she was seen a few months later she appeared to be normal, and there was no evidence of any damage to the nervous system.

BENJAMIN, Montreal, Canada.

A CASE OF AMAUROTIC FAMILY IDIOCY (TAY-SACHS' DISEASE). A. VENUTI and O. SANTONOCETO, Riv. di clin. pediat. **32**:21 (Jan.) 1934.

The author reports a case of amaurotic family idiocy in a girl, aged 13½ months. The parents were Italian Catholics with no Jewish ancestors. There were twelve siblings; two of them boys, the first and ninth children, had died of the same condition.

HIGGINS, Boston.

CLINICAL VALUE OF THE ESTIMATION OF THE CHLORIDES OF THE CEREBROSPINAL FLUID. M. TORELLO CENDRA, But. Soc. catalana de pediat. **4**:58 (April-June) 1931.

Eleven and one-tenth milligrams per liter were taken as the normal chloride content of the spinal fluid; variations of from 7 to 7.5 mg. were considered normal. Low chloride levels were found in persons with tuberculous meningitis, pneumococcic meningitis, epilepsy and lethargic encephalitis. Low spinal fluid chloride contents are pathognomonic of tuberculous meningitis if clinically there is definite meningitis with clear fluid.

Further study is suggested on the cause and effect relationship between increase of spinal fluid chlorides and increased pressure during a convulsive seizure.

WATSON, Elmhurst, Ill.

VALUE OF PSYCHOLOGIC EXAMINATION OF SCHOOL CHILDREN. CLAUDIO BASSOLS, But. Soc. catalana de pediat. **4**:114 (July-Sept.) 1931.

Psychologic examination is indispensable in the selection of abnormal persons and the classification of mental defectives, in vocational guidance and psychotherapy and as an aid in the discovery of genius.

WATSON, Elmhurst, Ill.

DIAGNOSIS OF TUMORS OF THE FOURTH VENTRICLE, WITH REPORT OF A CASE. M. TORELLO CENDRA, EDUARDO TOLOSA COLOMER and J. PUIG SUREDA, But. Soc. catalana de pediat. **4**:123 (July-Sept.) 1931.

A case of medulloblastoma of the fourth ventricle is reported, and the subject of tumors of the brain in children is discussed.

WATSON, Elmhurst, Ill.

USE OF IONTOPHORESIS IN MOTOR NERVE DISORDERS IN INFANCY. E. PERES CASANAS, Paidoterapia **12**:905 (Jan.) 1934.

The author believes that ionization is a new process by which to introduce medical substances into the body. He describes the mechanism of iontophoresis, remarking that when an electric current passes through the body it is not by conduction but by "convection," that is, at the cost of the transport of certain elements resulting from electrolytic dissolution. A scheme similar to the classic experiment of Lieduq is described to give an example of how the transport of ions takes place when the galvanic current passes.

Iontophoresis has increased the rate of healing and accentuated alleviation in degenerative processes of the nervous system. Four cases are described: one in which section of the terminal branches of the cubital nerve had been performed, one of dissociated paralysis of the seventh cranial nerve on the right, one of paralysis of the right leg and one of cerebromedullar polysclerosis.

HERRON, Spokane, Wash.

A CASE OF PACHYMENINGITIS. LUIS ALFREDO DIAZ GONZALEZ, Rev. chilena de pediat. **4**:1 (Jan.) 1933.

The author reports this rare condition in an infant aged 6 months. Early symptoms were fever, loss of appetite, continuous vomiting, generalized twitching, tense fontanels and drowsiness. Later lumbar puncture tentatively revealed hemorrhagic fluid. The same was obtained from a puncture of the fontanel, but at this point the fluid was under great pressure. Three successive punctures of the fontanel revealed the same condition. Wassermann reactions of the spinal fluid and the blood were positive. The coagulation time was normal.

Treatment consisted in the administration of calcium chloride, inunctions with mercurial ointment and the administration of yodovodyl. The infant recovered.

SCHLUTZ, Chicago.

UNILATERAL TOTAL ATROPHY OF THE OPTIC NERVE WITH SIGNS OF INVOLVEMENT OF THE PYRAMIDAL TRACT IN CHILDHOOD. P. VON KISS and I. TENYES, Arch. f. Kinderh. **101**:104 (Jan. 31) 1934.

This is a case report concerning a 15 year old child with atrophy of the optic nerve in the left eye and signs of involvement of the pyramidal tract. The left-sided blindness was considered to be due to retrobulbar neuritis. A differential diagnosis between multiple sclerosis and neuromyelitis optica could not be definitely established.

LEMASTER, Evanston, Ill.

DEMONSTRATION AND DETERMINATION OF LACTIC ACID IN THE SPINAL FLUID IN MENINGITIS. J. GELDRICH, Arch. f. Kinderh. **101**:108 (Jan. 31) 1934.

The lactic acid content of the spinal fluid was determined by the titration method of Embden in several cases of tuberculous meningitis. The same results were obtained by using the colorimetric method. Although the lactic acid content of the spinal fluid was always increased in meningitis, the lactic acid in the blood remained at a normal or low level. These findings support the contention that the decrease in spinal fluid sugar and the increase in lactic acid is a local chemical process occurring in the spinal fluid secondary to meningeal inflammation and is not affected by the blood. The determination of spinal fluid lactic acid is considered to be of value not only in distinguishing normal from pathologic spinal fluid but also in differentiating the various types of meningitis.

LEMASTER, Evanston, Ill.

ENTERITIS-POLIOMYELITIS AND ITS SIGNIFICANCE IN THE CLINICAL COURSE, PATHOGENESIS AND EPIDEMIOLOGY OF HEINE-MEDIN'S DISEASE IN YOUNG CHILDREN. E. MAYERHOFER, Arch. f. Kinderh. **101**:160 (Feb. 28) 1934.

Attention is directed to the frequency of gastro-intestinal symptoms preceding an attack of poliomyelitis. The author maintains that this initial gastro-enteritis is nonspecific and that it lowers the resistance of the gastro-intestinal tract so that poliomyelitis virus can enter the lymph and blood stream and cause an acute attack of poliomyelitis. To accept this theory of pathogenesis one must assume that the poliomyelitis virus is frequently present in the intestinal canal without causing any symptoms until the permeability of the intestinal wall is reduced and the virus is able to invade the entire body. If this theory is true, it is extremely important to avoid gastro-enteritis in young children, because of the danger of the poliomyelitis virus becoming active. The author cites a great deal of clinical material in favor of his views.

LEMASTER, Evanston, Ill.

FREQUENT SPORADIC APPEARANCE OF BULBOPONTINE FORMS OF PARALYSIS IN CHILDREN. F. BAMATTER, Arch. f. Kinderh. **101**:193 (March 31) 1934.

The author reports six cases of sporadic poliomyelitis showing isolated facial paralysis. The difficulties encountered in recognizing the paralysis as being due to poliomyelitis are discussed. In two cases the inoculation of monkeys confirmed the diagnosis. Along with the bulbopontine forms of paralysis, the author also saw several cases of poliomyelitis in which encephalitis and meningitic symptoms dominated the clinical picture.

LEMASTER, Evanston, Ill.

THE PRESSURE AND CHEMISTRY OF THE CEREBROSPINAL FLUID BEFORE AND AFTER THE REMOVAL OF LARGE QUANTITIES OF FLUID AND THEIR RELATIONSHIP TO CERTAIN DRUGS. K. HAUG and L. GÖTTKE, Arch. f. Psychiat. **99**:426, 1933.

The investigations reported in this article were undertaken to ascertain the relationship of the regeneration of the spinal fluid to the blood-cerebrospinal fluid barrier and also to determine the influence of certain drugs on both of these. Thirty-

seven experiments were carried out; the results indicated: 1. The composition of fluids removed from different parts of the canal shows marked variations. On the whole, the concentration of both crystalloids and colloids is greater in the lumbar than in the cisternal fluid. 2. The time of regeneration after the removal of fluids depends on the quantity removed, and for from 40 to 65 cc. it ranges from three to six and one-half hours. The speed of regeneration can be influenced by certain drugs, and this regeneration has a special relationship to the permeability for bromides. Without the administration of drugs, the speed of regeneration is directly proportional to the permeability; that is, with high permeability the regeneration is more rapid, and vice versa. Calcium causes decreased permeability and a decreased rate of regeneration. The same is true of phenobarbital. Atropine causes increased permeability but a decreased rate of regeneration. Theophyllinethylenediamine causes decreased permeability and an increased rate of regeneration. Methenamine causes increased permeability but does not tend to influence to any extent the rate of regeneration. A preparation containing solution of pituitary causes decreased permeability with a decreased rate of regeneration. During treatment with a fever-producing drug, the permeability and the rate of regeneration are decreased. The fact that the rate of regeneration and the permeability for bromides may be equally affected by some drugs but influenced in opposite directions by others tends to show that these functions are not always directly related. The authors conclude that their investigations point to the fact that the permeability for bromides as well as for other substances cannot be explained purely on the basis of dialysis but must be partly dependent on physiologic activities of the cells of the membranes.

MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

STUDIES OF A FAMILY AFFLICTED WITH HUNTINGTON'S CHOREA. M. RIGGENBACH and A. WERTHEMANN, Schweiz. Arch. f. Neurol. u. Psychiat. **31**:306, 1933.

The authors present data relative to forty-eight members and five generations of the family which they investigated. Nine persons were known to have Huntington's chorea; ten either had died prior to the usual age of onset or had not attained that age. No descendant of the members not afflicted had contracted the disease. Contrary to the general rule, those remaining free from the disease were well equipped mentally and physically, several being of superior intelligence. The nine suffering from Huntington's chorea showed much the same clinical picture. All but one deteriorated mentally; in some instances mental and emotional changes constituted the first manifestations of the disease. The one case reported in detail is of some forensic interest, since the patient killed his father four years after the appearance of choreiform movements. He was adjudged mentally incompetent and committed to a state hospital, where he died at the age of 48, seventeen years after the onset. Anatomically, the most marked changes were found in the small cells of the caudate nucleus and putamen; both these structures were greatly shrunken. Extensive changes were also found in the middle layers of the cerebral cortex. The degree of glial response closely approximated the extent of damage to the ganglion cells.

DANIELS, Denver. [ARCH. NEUROL. & PSYCHIAT.]

STATISTICAL STUDIES OF THE ETIOLOGY AND AGE OF ONSET IN EPILEPSY, WITH PARTICULAR CONSIDERATION OF EPILEPTIC TWINS. GERTRUD STROESSLER, Schweiz. Arch. f. Neurol. u. Psychiat. **32**:115, 1933.

Although 45 of 4,280 epileptic patients whose records were reviewed by Stroessler were twins, identical twins were encountered only twice; these and a pair of biovular twins furnished the only instances of epilepsy in both members of a pair. The average age at onset (13 years) and the proportion of cases of symptomatic epilepsy were approximately the same among the twins as in the entire series. Twin birth did not appear to predispose to epilepsy. A family

history of epilepsy was obtained in 22.6 per cent of the 4,280 cases, but direct antecedents, that is, parents or grandparents, were known to have had seizures in only 6 per cent of the cases.

DANIELS, Denver. [ARCH. NEUROL. & PSYCHIAT.]

A CASE OF HEMANGIOMA CEREBRI. A. v. WESTRIENEN, Maandschr. v. kindergeneesk. **3**:242 (March) 1934.

A case of this condition in a boy, aged 6 years, with status epilepticus, is reported.

VAN CREVELD, Amsterdam, The Netherlands.

CONVULSIONS AS THE FIRST SYMPTOM OF EPILEPSY. J. J. H. M. KLESSENS, Maandschr. v. kindergeneesk. **3**:307 (May) 1934.

In this article there is an extensive discussion of the modern conceptions of the etiology of epilepsy and of the difficulties in deciding whether convulsions in children indicate epilepsy. Some examples are given to demonstrate that convulsions coming on with fever do not exclude the possibility of beginning epilepsy. The familial occurrence of other disturbances in vasoconstriction may help in the diagnosis. Treatment in cases of epilepsy caused by a cerebral lesion must consist in combating the increased irritability of the brain, and in cases of beginning idiopathic epilepsy, in combating the vasoconstriction.

The effect of the ketogenic diet and the hunger diet is principally due to a favorable influence on vasolability.

VAN CREVELD, Amsterdam, The Netherlands.

MULTIPLE SCLEROSIS IN TWINS. A. M. LEGRAS, Nederl. tijdschr. v. geneesk. **78**:174 (Jan. 13) 1934.

The occurrence of disseminated sclerosis in identical twins, now 24 years old, gives reason to doubt the usual assumption that this disease is infectious.

VAN CREVELD, Amsterdam, The Netherlands.

INFLUENZAL MENINGITIS. E. GORTER, Nederl. tijdschr. v. geneesk. **78**:1190 (March 17) 1934.

A case of this condition is reported. Temporary recovery followed the treatment advised by Ward and Fothergill.

VAN CREVELD, Amsterdam, The Netherlands.

BRACHYDACTYLIA, NYSTAGMUS AND CEREBRAL ATAXIA AS A FAMILIAL SYNDROME. A. BIEMOND, Nederl. tijdschr. v. geneesk. **78**:1423 (March 31) 1934.

This is a description of a familial syndrome of a particular form of brachydactylia (hypoplasia of one of the metacarpals and of one of the metatarsals), nystagmus (and other deviations of the eye) and cerebellar ataxia. The antecedents of the mother showed manic-depressive psychosis in two generations; on the father's side there was an inherited anomaly of the eyes. The author explains the condition by a concurrence of hereditary factors, as is also done in the case of the syndrome of Laurence-Biedl.

VAN CREVELD, Amsterdam, The Netherlands.

PURULENT MENINGITIS DUE TO BACILLUS ENTERITIDIS GÄRTNER. H. G. RUPERT, Nederl. tijdschr. v. geneesk. **78**:1763 (April 21) 1934.

A case of this disease is reported in a child, aged 3½ months. The child was probably infected by the father, a butcher.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the Eye

STRABISMUS WITH SOME CONSIDERATION OF METHODS FOR ITS CORRECTION. J. W. JERVEY JR., J. South Carolina M. A. **30**:32 (Feb.) 1934.

As soon as a squint is recognized, treatment should be begun. All squints develop before the eighth year, unless they are due to a lesion of the central nervous system or to trauma or tumor. The use of atropine and occlusion of the good eye are advised. The author concludes by describing the Jamison recession operation.

WESTON JR., Columbia, S. C.

THE CONTROL OF SCHOOL MYOPIA. ARNOLD SORSBY, Brit. M. J. **2**:730 (Oct. 21) 1933.

The author gives a brief summary of the attempt which has been made and the theories which have been advanced for the control of myopia in the school child, laying special stress on the work of Hermann Cohn. In various countries reports have been brought out showing reduction in the incidence of myopia, which is more pronounced in girls than in boys. These results are probably due to improved hygienic conditions, especially lighting, improved texts and the partial abolition of work which requires the pupil to bend his head over the book. It is well known that whatever the condition of the eye may be at birth, during infancy or in early childhood there is a tendency for it to become hyperopic as life advances. The myopic eye develops almost invariably before the age of 8 years. It represents the process of rapid increase in refraction supervening on the normal adjustment which aims at the theoretically emmetropic eye.

An outline is given of the various theories of myopia, and stress is laid on heredity as a factor, but this cannot be considered the cause of all myopia. The plea is made that one go into the matter more carefully and more extensively. Only when the rate of development of the eye and the peak of the physiologic development is determined can one begin to correct the defect in large numbers of cases.

ROYSTER, University, Va.

STRABISMUS IN CHILDHOOD. J. A. VAN HEUVEN, Maandschr. v. kindergeneesk. **3**:120 (Dec.) 1933.

This article is a survey of the different forms of strabismus and their treatment. The author warns against too early operation and believes that surgical intervention should not be carried out before the ninth year.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the Ear, Nose and Throat

DEAFNESS: FREQUENCY, CLASSIFICATION AND SOME OF THE COMMON CAUSES. STANWOOD E. FISHER, Maine M. J. **24**:11 (Jan.) 1934.

The prevention of deafness is concerned with the detection of impaired hearing in its earliest stages. Even in childhood this condition involves economic loss by necessitating repetition of grades in school and the maintenance of public institutions for the extremely deaf.

Of 2,750,000 men examined for the draft, 32,000, or 1.5 per cent, were found to have aural defects. About 10 per cent of school children suffer from some defect in hearing. The United States census of 1930 reports 57,084 deaf-mutes who either were born deaf or supposedly lost their hearing before the age of 8 years.

Elimination of causes and early detection of cases, with prompt institution of therapeutic measures, are most important in prevention, because 75 per cent of cases can be arrested or benefited if seen early. Causes comprise: acute contagious

diseases, enlarged tonsils and adenoids, infections of the upper respiratory tract, abnormalities of the nasal passages and sinuses, the marriage of persons with a family history of deaf-mutism or otosclerosis, industrial and other noises, suppuration of the ear, syphilis, unsanitary swimming pools and detrimental drugs, such as quinine, salicylates and arsenicals.

A simple test calls for the hearing of an ordinary Ingersoll watch at a distance of 48 inches (1.2 meters) and of the whispered voice at 20 feet (6.09 meters). In examining large groups, the audiometer may be used by school nurses to screen out the pupils with impaired hearing in a given group.

Most children complain of deafness only after they are well along in school age. However, those affected repeat more grades than other children. Reticence and sensitiveness often result from the poor hearing. Progressive deafness due to fixation of the conductive apparatus and deafness produced by degeneration of the eighth nerve are almost never found in children. Three fifths of the cases of deaf-mutism are accounted for by heredity and consanguineous marriages. Acquired deafness is found in less than half the children in public institutions for the deaf. This form is usually of the tubotympanic type, is not so severe as the congenital form, is intermittent and is traceable to unfavorable climate inducing frequent colds, with the involvement of sinuses. Undernourishment may have some etiologic relationship to deafness.

Deafness of middle age and senile deafness are also discussed.

GRAVES, New York.

TUBERCULOUS DISEASE OF THE MIDDLE EAR AND MASTOID. H. ROSS SOUPER, Edinburgh M. J. **41**:154 (March) 1934.

This disease is rare in adults but not so rare in children. Thirty-six cases are reported for a period of eleven years in the Royal Aberdeen Hospital for Sick Children. In 50 per cent of the children under 1 year of age the suppurative otitis media was tuberculous, the incidence being more probable the younger the child, as was found in the Edinburgh survey.

Otitis of this origin begins insidiously and painlessly, the discharge being the usual sign to call attention to the ear. Swelling of the mastoid or facial paralysis brings the child to the hospital.

The characteristic pathologic changes are large perforations and granulations; the discharge, which at first is thin and flaky, becomes purulent, fetid and blood-tinged, occasionally containing bacilli. Osseous involvement is striking, with its frequent complications of facial paralysis. About 50 per cent of Souper's patients showed paralysis, even before operation. Enlarged periauricular glands were noted in 77 per cent of his cases, the condition of the preauricular region being of diagnostic significance.

The author's patients seldom had a personal or family history suggestive of tuberculosis. Not all the children presented an appearance of severe illness. Infection is thought to reach the middle ear by way of tuberculous milk entering the eustachian tube; a percentage of 80 or more of the babies in Scotland being bottle-fed.

The disease is confirmed by finding the bacilli in the discharge, by inoculation of laboratory animals or, most commonly, by typical histopathologic osseous tissue taken at operation.

The operation is radical, the mortality being 50 per cent. Most deaths are due to tuberculous meningitis or postoperative shock. The general condition of the child has an important bearing on the diagnosis, even if widespread necrosis of bone is present. Thirteen children were alive from eight months to eight and one-half years after the operation. In seven of these the infection proved to be tuberculous.

NEFF, Kansas City, Mo.

Diseases of the Skin

DRUG ERUPTIONS: II. DERMATITIS ECZEMATOSA DUE TO DRUGS. M. B. SULZBERGER and FRED WISE, Arch. Dermat. & Syph. **28**:461 (Oct.) 1933.

The cutaneous eruptions discussed in this article were due to butesin picrate, to a proprietary ointment containing iodine and to mercurochrome. A patient may be sensitive to either or both of the components of butesin picrate. The authors give the following three phases in the sensitization of the skin to an eczematous type of reaction: (1) "a period of refractoriness," in which the patient may use the drug for days to years without untoward effects; (2) "a period of incubation of sensitization," which for butesin picrate they found to be from seven to thirteen days; this period is relatively constant for a given drug and is comparable to that of serum sickness and arsphenamine hypersensitiveness, and (3) "a period of development of reaction," which may last for hours to days before the rash begins to subside. The patch test was used to prove sensitization in the cases cited.

DULIN, Iowa City.

PSEUDOXANTHOMA ELASTICUM AND ANGIOID STREAKS: A DISEASE SYNDROME WITH COMMENTS ON THE LITERATURE AND THE REPORT OF A CASE. GEORGE M. LEWIS and M. B. CLAYTON, Arch. Dermat. & Syph. **28**:546 (Oct.) 1933.

The authors reviewed the literature and found sixteen cases in which pseudoxanthoma elasticum and angioid streaks occur together. The article includes the report of a case and illustrations showing the patient, the fundus of the eye with the angioid streaks and the pathologic changes in the skin. They suggest the term elastosis atrophicans to designate this disease syndrome, since neither pseudoxanthoma elasticum nor angioid streaks is adequate. The many theories regarding the etiology of the angioid streaks are given.

DULIN, Iowa City.

ACNE IN A CHILD AGED TWO YEARS. A. M. H. GRAY, Proc. Roy. Soc. Med. **27**:292 (Jan.) 1934.

The lesions were localized to the cheeks and consisted of a number of discrete comedones, with a few papules of acne and deep-seated nodules. There was a history of camphorated oil having been rubbed on the child's chest at the age of 3 months, but none was used since. Lesions of this type have been noticed on the face after the application of oil to the chest. The author was not able to grow the acne bacillus in this case; only gram-positive cocci and bacilli were present. Clinically, it is difficult to distinguish between such a case and one of ordinary acne, and the similarity raises the interesting question as to the origin of ordinary acne.

WILLIAMSON, New Orleans.

TREATMENT OF PALPEBRAL ANGIOMAS BY ELECTROLYSIS AND RADIUM. MANUEL MARIN AMAT, Arch. de oftal. hispano-am. **32**:604 (Nov.) 1932.

Two patients with palpebral angiomas were treated, respectively, by electrolysis and by radium, with excellent results. Comparing both methods, Amat concludes that, in accordance with present therapeutic knowledge, radium and bipolar electrolysis constitute the most efficient means at one's disposal in the treatment of palpebral angiomas. When the angiomas are circumscribed to the lids, with only a slight invasion of the adjacent regions, he prefers electrolysis. When there is great invasion of the surrounding areas, especially if the condition is complicated with hemorrhages, radium is to be preferred. The article is illustrated.

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

A Case of Infantile Acrodynia. E. Filguerias, Pediatria, Rio de Janeiro **1**:35 (March) 1934.

A child 16 months old with this condition improved when fed a diet rich in vitamins, leguminous vegetables and bananas.

Sanford, Chicago.

Tuberculous Etiology of Erythema Nodosum. L. Rotnes, Acta dermat.-venereol. **14**:394 (Dec.) 1933.

According to the author, tuberculosis plays a prominent rôle in the etiology of the great majority of cases of erythema nodosum in children. However, the question of the tuberculous origin of this condition in adults is not settled. He reports the cases of four sisters, two adults and two children, living at home together, in whom typical erythema nodosum developed at the same time. All of them gave strongly positive Pirquet reactions. In the children roentgen examinations disclosed involvement of the lungs. In the two adults roentgen examinations gave negative results. The husband of one of the sisters, who was tuberculous, had come to live with them shortly before they all fell ill; he apparently infected at the same time three other children in addition to the sisters. He died a few months later. The author believes that tuberculosis was the main factor in the etiology of these cases of erythema nodosum.

Astrachan, New York. [Arch. Dermat. & Syph.]

Telangiectasia Haemorrhagica Hereditaria. F. Foldvari, Acta dermat-venereol. **14**:427 (Dec.) 1933.

Telangiectasia haemorrhagica hereditaria is characterized by: (1) heredity; (2) a tendency to the formation of telangiectasia and angiomas, mostly on the face, buccal mucosa, tongue and septum of the nose, and (3) hemorrhages, which occur mostly from the nose. It was first described by Osler in 1907, and two hundred and seven cases have been reported. The condition may be transmitted to both sexes and carried through many generations. The hemorrhages, which appear usually at the age of puberty, may be so frequent and severe that anemia or death results. The disease has nothing to do with hemophilia. The author reviews the literature on the subject. He reports a case of a family in which the patient, his father, an uncle, a brother, a sister and a daughter of the sister showed symptoms of telangiectasia haemorrhagica hereditaria. He also discusses the therapy of this condition.

Astrachan, New York. [Arch. Dermat. & Syph.]

A Skin Disease Caused by Officinal Leaves. J. A. Verbunt, Nederl. tijdschr. v. geneesk. **77**:4436 (Sept. 30) 1933.

The author describes a dermatosis *e causa externa* found in the Netherlands East Indies, caused by a great number of pieces of leaves which the patients had pasted on their skin. These cause local itching and such irritation of the skin that this dermatosis medicamentosa may be easily mistaken for frambesia or syphilis. The author discusses the differential diagnosis and points to the difficulty in obtaining an exact anamnesis from the natives.

van Creveld, Amsterdam, The Netherlands.

Surgery and Orthopedics

The Congenital Pericolic Membrane Syndrome, Often Misnamed Chronic Appendicitis; a Preliminary Report of Observations. W. H. Bueermann, Am. J. Digest. Dis. & Nutrition **1**:196 (May) 1934.

The author lists the types of pericolonic membranes and describes the syndrome that leads to the diagnosis of congenital pericolonic membranes. Many cases of so-called chronic appendicitis or chronic cholecystitis are actually cases of this

condition. This has been proved in cases in which there was a previous operation; the symptoms were unrelieved until the pericolonic membranes were released at a later operation.

Pain in the right side on exercise is an important factor in the diagnostic syndrome of congenital pericolonic membranes, while other symptoms are: constipation, intestinal colic, nausea and vomiting, failure to gain weight, capricious appetite and variable periods of nervous irritability. These symptoms are especially significant when present after an increase in activity.

Ordinary roentgenograms appeared not to help in making the diagnosis, but a special roentgen technic is presented.

The article is well written and forceful.

MORRISON, Savannah, Ga.

OSTEOMYELITIS OF THE ILIUM. CARL E. BADGLEY, Arch. Surg. **28**:83 (Jan.) 1934.

Acute osteomyelitis of the ilium is generally regarded as a rare lesion with a grave prognosis. A high percentage of the survivors of the acute infection present severe lesions of the hip joint, including bony ankylosis, fibrous ankylosis or pathologic dislocation of the hip. In the author's twenty-four cases, as well as in the cases reviewed from the literature, children and adolescents were more likely to have this type of infection than older persons. Trauma is frequently cited in the histories obtained, and the organism which is chiefly responsible is Staphylococcus pyogenes-aureus.

The factors involved in arriving at a diagnosis are thoroughly considered, and the treatment for the different types of osteomyelitis is outlined. Seventeen of the author's twenty-four patients have been completely cured, which disproves the earlier reports that this infection necessarily has a grave prognosis.

KAISER, Rochester, N. Y.

DIGESTION OF BONE BY LARVAE OF PHORMIA REGINA; ITS RELATION TO BACTERIA. I. H. MASERITZ, Arch. Surg. **28**:589 (March) 1934.

The use of living maggots as a therapeutic measure in osteomyelitis has brought about early complete healing of infections of the bone. The cause of this rapid healing has remained an unsolved problem. It was thought that the end-results were possibly due to the ingestion of dead tissue by the maggots or to the liberation of an enzyme. The author undertook an investigation of larval digestion which might aid in a better understanding of the therapeutic use of living maggots. The excreta of the larvae of Phormia regina were found to contain an enzyme capable of digesting the organic portion of bone. The proteolytic enzymes of the intestines and the excreta were also capable of digesting white fibrous tissue collagens and gelatin. These enzymes were fairly stable, but showed no specificity. The author, however, was unable to confirm the claims of previous workers in showing that emulsions of maggots revealed any bactericidal action, agglutination, lysis or digestion of bacteria.

KAISER, Rochester, N. Y.

MESENTERIC CYSTS, WITH THE REPORT OF A CASE. D. ROSS and C. I. MEAD, Canad. M. A. J. **30**:262 (March) 1934.

About 400 cases of mesenteric cysts have been reported altogether in the medical literature. Warfield suggested that most cases can be classified into one of two groups—embryonic retroperitoneal rests of tissue, such as germinal epithelium and ovary, or displaced intestinal tissue sequestrated from embryonic intestinal diverticuli or from the vitelline duct. Mesenteric cysts are more common during the fourth decade of life, although cases have been reported at all ages. There are no constant symptoms. The treatment is always surgical.

The case reported is that of a boy, aged 8 years. He had never been well. Three years before entrance to the hospital he had had an appendectomy because of chronic constipation and vague abdominal pains. At the time of examination he complained of severe, steady abdominal pain without localization.

The essential physical finding was an egg-shaped tumor in the lower part of the abdomen, extending from the symphysis pubis to the umbilicus. Operation revealed a large, thick-walled cystic mass. This was aspirated, and 600 cc. of an amber-colored fluid was obtained. When this was delivered another bilateral cystic tumor occupying the whole of the left upper quadrant was found. The cysts arose from the same region of the mesentery; they were closely adherent to the bowel, but did not communicate with it.

A careful pathologic description of the specimen is given. The results of pathologic examination suggest that the mesenteric cysts in this case were of enteric origin and were remnants of intestinal diverticuli present during embryonic life.

MOORE, Omaha.

PRIMARY PSOITIS; A REPORT OF ELEVEN CASES IN CHILDREN AND ADOLESCENTS. PIERRE INGELRANS and JEAN MINNE, Rev. d'orthop. **20**:577 (Nov.) 1933.

Primary inflammation of the psoas muscle or its sheath may follow superficial infection or a blow on the leg. The infection reaches the psoas muscle through the lymphatics or blood stream. Such primary psoitis is independent of lesions in either the neighboring bone or the neighboring organs. The leg of the affected side is slightly flexed, abducted and externally rotated. Adduction, internal rotation and extension of the leg cannot be carried out. A definite mass may be palpable over the lower border of the muscle. This mass may be tense or fluctuating. Pain may be present on pressure over the lesser trochanter, and when present is said to be diagnostic. In diagnosis differentiation must be made between suppurative arthritis and appendicitis. In suppurative arthritis of the coxofemoral joint the hip is fixed. In psoitis slight motion is possible. If treatment is not instituted early, coxofemoral arthritis, hemorrhage from the abscess or a fistulous tract may develop. Death may be due to pyemia, peritonitis or thrombosis of the iliac veins. Treatment consists in early incision of the abscess, followed by physical therapy.

RYAN, Vancouver, Canada.

MOST FREQUENT OPERATIVE PROCEDURES NECESSARY FROM INFANCY TO THE FIRST YEAR OF LIFE. ANDRES MARTIN, Paidoterapia **12**:989 (Feb.) 1934.

During the first day of life two operative procedures are sometimes necessary—that for umbilical hernia and that for imperforate anus. Both these operations must be performed immediately and preferably without the use of an anesthetic. Babies with congenital stenosis of the urethra must also be operated on at once, but in exstrophy of the bladder operation is performed later, if at all.

During the following weeks and months the operative procedures include that for congenital hypertrophic pyloric stenosis, when this does not respond to medical management. Babies with intermittent inguinal hernia should not be operated on, and those with inguinal hernia that is permanent but that can be reduced should be treated by a truss bandage first. Hydrocele rarely requires an operation.

Babies with intussusception must be operated on the day on which the diagnosis is made. Meckel's diverticulitis is usually an acute process. There is no emergency requiring operation in cases of encephaloceles. In harelip and cleft palate operation is performed before four months. The aspiration of pus, then an operation, if necessary, are done in empyema. Infants with suppurative arthritis and osteomyelitis are operated on after the diagnosis is made.

HERRON, Spokane, Wash.

A CASE OF RADIAL PARALYSIS FOLLOWING FRACTURE. J. TRENCHS CODONES, Paidoterapia **12**:1003 (Feb.) 1934.

A girl, aged 7, fell on the stairs and fractured the lateral condyle of the humerus. Healing took place, and then the typical picture of radial paralysis appeared, owing to the envelopment of the radial nerve in the fibrous tissue of

healing. The radial nerve was dissected free from scar tissue, and rapid return of function and sensation occurred. Such a complication of this type of fracture should always be held in mind, and parents should be told of its possibility.

HERRON, Spokane, Wash.

TUBERCULOSIS IN THE ETIOLOGY OF KOEHLER'S DISEASE. SUAREZ, Pediatría españ. **22**:393 (June) 1933.

Köhler's disease of the tarsal scaphoid, pathologically, is without doubt a disturbance of vascularization. Diverse causes may produce the disease. Some cases are undoubtedly of infectious origin. Tuberculosis must always be considered as a possible cause.

SCHLUTZ, Chicago.

ETIOLOGY OF APPENDICITIS IN INFANCY. HERBERT VOLKMAR, Arch. f. Kinderh. **101**:142 (Feb. 28) 1934.

A case of acute appendicitis in a 3 week old infant is reported. Death was due to perforation of the appendix with resulting peritonitis. The difficulties encountered in making the diagnosis are discussed. Of the various theories of the etiology of appendicitis the author favors the view that in infancy infections of the upper respiratory tract, particularly of the grippal type, are apt to lead to appendicitis.

LEMASTER, Evanston, Ill.

PROPHYLAXIS IN CHILDHOOD. FRANZ HAMBURGER, Arch. f. Kinderh. **101**:182 (Feb. 28) 1934.

The prophylaxis of phimosis and preputial adhesions is discussed. The author advises manual stretching of the prepuce backward over the glans and manually breaking up the adhesions in early infancy. If acute balanoposthitis arises, correction of the phimosis and preputial adhesions is done immediately after the acute symptoms have subsided.

LEMASTER, Evanston, Ill.

PATHOLOGIC STATES IN TWINS, WITH SPECIAL CONSIDERATION OF SURGICAL AND ORTHOPEDIC ABNORMALITIES. K. E. HERLYN, Beitr. z. klin. Chir. **157**: 421, 1933.

The author discusses the problem of heredity and environment in pathologic states found in twins. He comes to the conclusion that further investigation will clear up this problem to a great extent.

RUBIN, Boston.

OSTEOCHONDRITIS DEFORMANS JUVENILIS CUBITI. WINTERSTEIN, Beitr. z. klin. Chir. **157**:527, 1933.

Cases of this disease are reported, with a series of roentgenograms showing progress of the condition. The author points out disturbances of ossification of the capitellum of the right humerus. He claims that this condition is aggravated by trauma due to excessive motion and exercise. If there is suspicion of this trouble, participation in sports should be forbidden.

RUBIN, Boston.

MANAGEMENT OF OSTEOMYELITIS WITH MAGGOTS. O. SCHURCH, Beitr. z. klin. Chir. **158**:613, 1933.

The author has been using this method for several years and has come to the conclusion that it is possible to use it in a surgical clinic without great difficulties.

However, even though satisfactory results have been obtained, further work and experimentation should be done before definite proof of specific cure will be evident with the live maggots and extracts.

RUBIN, Boston.

INFLUENCE OF VITAMINS ON ACUTE INFECTIONS. HANS JOACHIM LAUBER, Beitr. z. klin. Chir. **158**:633, 1933.

The author has previously shown that vitamin A added to the diet causes definite improvement in the healing of wounds. He also believes after experimentation that this vitamin influences acute infections favorably and that surgeons should understand and use vitamin therapy, whenever indicated.

RUBIN, Boston.

EFFECT OF "ACIDOSIS" (ACID-FORMING DIET) ON THE HEALING OF WOUNDS. C. REIMERS and H. WINKLER, Deutsche Ztschr. f. Chir. **241**:313 (Sept. 25) 1933.

The authors worked with dogs and corroborated the studies of other investigators that wounds release carbon dioxide to the atmospheric air and that bandages exert no appreciable influence on this secretion. Quantitative studies are reported. The reactions of the secretions of the wound are of minor importance from the standpoint of healing. Wounds heal with either acid or alkaline secretions. The clinical observation that acidosis favors the healing of wounds is confirmed. In severely infected wounds an average time of healing of eleven days was reduced to eight or nine days by the oral administration of ammonium chloride. Studies are reported showing the chemical effect of the ammonium chloride on the secretions of wounds. The difference in results between artificial and diabetic acidosis could not be explained, since it was not possible to produce true diabetic acidosis in dogs by extirpation of the pancreas.

GLASER, Rochester, N. Y.

RUPTURE OF AN APPENDICAL ABSCESS INTO THE BLADDER, WITH DISCHARGE OF ASCARIDES AND FECALITHS IN THE URINE. G. RINTELEN, Deutsche Ztschr. f. Chir. **242**:185 (Dec. 28) 1933.

Rupture of an appendical abscess into the bladder is rare. About forty cases have been described by various authors. The bladder is the least likely of all organs to be perforated as the result of an appendical abscess. The author describes the case of a 3 year old boy who had fever, abdominal pain and burning on urination for fourteen days. The abdomen was rigid and tender on pressure, especially over the bladder. The urine was cloudy and contained large numbers of fecal bacteria. On one occasion a living specimen of Ascaris lumbricoides was passed through the urethra, and on another a fecalith. The bladder was filled with 20 per cent sodium bromide, and a fistula leading from the bladder toward the cecum could be demonstrated by the roentgenogram. The diagnosis was confirmed by operation. The child died of general peritonitis the day after.

GLASER, Rochester, N. Y.

PHIMOSIS AND PSEUDOPHIMOSIS IN CHILDHOOD. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **77**:5483 (Dec. 9) 1933.

This article deals with the rôle of phimosis in the production of urinary obstruction in infants and young children. By phimosis is understood narrowing of the preputial opening, which prevents retraction either altogether or with great difficulty. In infants and children retraction is also often hindered by inflammatory swelling of the prepuce or by persisting concretion between the prepuce and glans, which is normal in fetal development. The signs and symptoms and the nonoperative methods of treatment are discussed. The indications for circumcision, which in some cases cannot be avoided, are described.

VAN CREVELD, Amsterdam, The Netherlands.

Miscellaneous

PHYSICAL EXAMINATION OF THE CHILD. W. L. CRAWFORD, Illinois M. J. **65**:49 (Jan.) 1934.

The various methods and procedures of physical examination which Crawford believes advisable for determining the presence and eliciting the etiologic factors of malnutrition and undernutrition are discussed and reviewed.

BARBOUR, Peoria, Ill.

FATIGUE IN SCHOOL CHILDREN. CHARLES G. KERBY, J. Pediat. **4**:322 (March) 1934.

This study concerns thirty-two children, from 7 to 15 years of age, who were brought to the physician because of persistent fatigue, inability to carry on the usual duties at school and lack of interest in customary activities. One group of twenty-two children showed a favorable response to such measures as adequate periods of rest, correction of minor ailments and psychotherapy. The other ten children showed no improvement under this regimen. However, in spite of negative physical findings, the children of this group had low basal metabolic rates. The administration of small doses of desiccated thyroid gland daily by mouth produced excellent results.

LEMASTER, Evanston, Ill.

THE RELATIONSHIP OF HOME AND HOSPITAL IN THE MANAGEMENT OF SICK CHILDREN. A. B. SCHWARTZ, J. Pediat. **4**:431 (April) 1934.

The author makes a plea for closer cooperation between the children's hospital and the home in the management of the ill child. Whenever possible, the ill infant should be cared for in the home, the parents being taught the proper care of the child. Infants and children should be sent to the hospital only when a special technic which is unavailable at home is indicated. No matter how successful therapy in the hospital may be, it cannot be permanent unless the home from which the child comes is prepared to follow the plan initiated in the hospital. Adequate hospital service includes not only the care of the ill child while in the hospital, but also follow-up supervision of the child in his home environment.

LEMASTER, Evanston, Ill.

NUTRITIONAL CONTROL OF DENTAL CARIES. EWING C. MCBEATH, New York State J. Med. **33**:1087 (Sept. 15) 1933.

This article is part of a symposium on dental conditions as they affect general health.

AIKMAN, Rochester, N. Y.

A CASE OF MATERNITY AT SEVEN YEARS OF AGE. HILDA KEANE, Brit. M. J. **2**:567 (Sept. 23) 1933.

This report came from the Victoria Zanana Hospital at Delhi, India, and concerns a Mohammedan girl, unmarried. Her age was 7 years, which was confirmed by the municipal birth records. The height of the child was 3 feet and 11 inches (119.4 cm.) and the weight was 3 stones and 6 pounds (21.8 Kg.). The milk teeth were still present, except the first molars and the right lower incisor; the left lower incisor was just erupting in front of the milk tooth. The patient had never menstruated. Labor started, but since the pelvic measurements were very small the head did not engage, and cesarean section was performed. A living child weighing 4 pounds and 3 ounces (1,899.4 Gm.) was delivered. The mother nursed the baby for nine months.

The author asks the following questions: Is this the earliest recorded case of pregnancy (*a*) going to full term? (*b*) in which delivery was by cesarean section and (*c*) in which the child was entirely breast fed?

ROYSTER, University, Va.

DENTAL DECAY IN MAN. J. SIM WALLACE, Bur. Internat. Humanitaire Zoophile, Geneva, 1934.

This essay was awarded second prize in a competition initiated by the International Humanitarian Bureau on the subject of the uselessness and cruelty of experiments on dogs and the best means of preventing dental decay. The contest was in the nature of a counter-competition to that sponsored by the International Dental Federation, which offered a cash prize and a gold medal for competitive research requiring experimental studies on the teeth of dogs.

The article is divided into three parts, the first of which is a historical review of early studies concerning the nature and etiology of dental caries. The second is a dissertation, "The Best Means of Preventing Dental Decay in Man." In this division the author offers evidence from his own studies in a series of fourteen patients and statistical data from reports of recorded dental conditions in children in schools and institutions in the United Kingdom. Briefly, his argument is that dental caries is due to the production of acid by the fermentation of débris of food of a "non-detergent carbohydrate nature" which is permitted to collect and remain on the surfaces of the teeth. The remedy, he believes, lies in the natural cleaning of these surfaces by a diet containing fibrous foods and artificial cleaning by means of the tooth-brush and oral prophylaxis.

The third portion is an elaboration of the author's belief in the "uselessness of animal experiments," the "harmful effects of which will be felt throughout life by the rising generation." This section is largely devoted to a critical review of the work of E. Mellanby and M. Mellanby and the "adulation of the Medical Research Council." A bibliography of sixty-four references and an appendix listing certain foodstuffs which are efficacious in the prevention of dental caries, owing to their fibrous quality, are furnished.

NOYES, Chicago.

HEIGHT, WEIGHT AND NUTRITION: OBSERVATIONS FROM THE ISLE OF ELY. THOMAS C. LONIE, J. Hyg. **34**:131 (Feb.) 1934.

More than five thousand children in elementary schools were examined in an investigation to determine normal standards of weight and height and to discover the extent of malnutrition.

Among younger children, boys are taller than girls, but girls are taller than boys from 10 to 14 years of age, 14 years being the age limit of those examined. Girls were also definitely heavier than boys after the eleventh year. Weight is much more variable than height, both variations increasing as the children grow older. Boys are heavier than girls at any given height except 56¾ and 57¾ inches (144.1 and 146.7 cm.). The more rapid growth of older girls is explained by the earlier onset of puberty in girls. In 8 per cent of the boys and 13.2 per cent of the girls examined the weight was 10 per cent or more below the mean weight for their height.

JANNEY, Wauwatosa, Wis.

POISONING BY ACETIC ACID. W. F. TCHERWAKOFF and S. E. LEWINTOFF, Arch. de méd. d. enf. **37**:257 (May) 1934.

During the past few years cases of acetic acid poisoning of infants and young children, not only through accidental administration but also from criminal motives, have been reported with increasing frequency. Numerous instances, especially in Russia, have aroused the attention of the public, and an extensive article on this unusual topic is offered by the director of the medicolegal institute at Minsk. The physical and chemical properties of acetic acid; its toxic effects, especially in infancy, and the postmortem observations are carefully reviewed. The histories of fifty-seven patients treated at the infant's clinic of the University of Russia are given; death was accidental in thirty of this number and for the most part occurred in children from 2 to 3 years of age.

AMESSE, Denver

ACUTE POISONING THROUGH THE USE OF A CAMPHORATED OIL ENEMA. EDUARDO DE BONI, Arch. de pediat. d. Uruguay **4**:401 (Sept.) 1933.

An enema of 100 cc. of camphorated oil given to a child 3 years old and representing the introduction of 5 Gm. of camphor resulted in symptoms of acute poisoning. These consisted in extreme pallor, visual disturbance, difficulty in speech, severe convulsions with loss of consciousness, vomiting, rapid breathing and finally profound sleep. Consciousness returned within twenty-four hours, and the infant made a complete recovery.

SCHLUTZ, Chicago.

MOTHERS' AND INFANTS' WELFARE CENTERS. G. A. ALFARO, Bol. Inst. internac. am. de protec. a la infancia **7**:174 (Oct.) 1933.

The author recalls the acknowledged principle that infant welfare is possible only if the welfare of mothers is established as well.

The care of mothers is required not only during pregnancy but also during and after childbirth. Good care in these periods tends to prevent all accidents causing maternal and infant mortality.

It is desirable that the different institutions for the protection of mothers and infants be organized on a basis of intimate cooperation, which would increase their efficiency. For many years the author has been aiming at the unification of all such services under a central direction and is happy to acknowledge that, in spite of all the obstacles he met with when presiding over the Council of Public Health in his country, he was able to create the Mothers' and Infants' Welfare Centers, which comprise: obstetric, infants' and antivenereal clinics, a small maternity hospital, obstetric home care, a *goutte-de-lait* and *crèche,* a children's clinic, social service for mothers and children and, in some districts, an antimalarial clinic, a mothers' dining-room and a home for neglected children.

The French government, for the purpose of arriving at the best and most economical solution of the problem, intends to unify all departmental services, creating maternal and infants' welfare centers with the same aim as that which inspired the organization of such centers in the Argentine Republic many years ago.

AUTHOR'S SUMMARY.

SEVENTH INTERNATIONAL CONFERENCE OF AMERICAN STATES; SOCIAL PROBLEMS. Bol. Inst. internac. am. de protec. a la infancia **7**:248 (Jan.) 1934.

Child welfare conferences in America have almost always assumed a general character, including all problems of this subject in their discussions. Six international child welfare congresses (Buenos Aires, 1916; Montevideo, 1919; Rio de Janeiro, 1922; Santiago, 1924; Habana, 1927, and Lima, 1930) and fifteen national congresses have met all over the Continent, and many other conferences of a wider scope have included in their programs and carefully discussed the problems of childhood. This shows the interest aroused in these countries by all subjects connected with child welfare and the desire to study them from an American point of view, in accordance with the environment, resources and possibilities of this country.

These conferences have had excellent results because of the study that has resulted in every country, the exchange of information that has been brought about and also the public and private agencies and institutions that have consequently been established, for nowhere have the problems been solved in theory only. The author mentions several institutions which were founded as a result of such conferences, the first of which is the United States Children's Bureau, established in 1912 by a resolution of the first White House Conference of 1909, and the last of which is the International American Institute of Child Welfare, which originated at the initiative of Dr. Luis Morquio at the Second Pan-American Child Welfare Congress, in Montevideo, and the founding of which was ratified by the Rio de Janeiro and Santiago congresses.

Founded in 1928, the Institute has established relations with all American countries; it has founded a public library, with a considerable number of filed and cataloged publications, and it publishes a quarterly bulletin, the last issue of which was the second number of volume VII. Important resolutions, representing valuable suggestions, were proposed at the Lima Congress (1930); these would have been carried out had it not been for the fact that, due to various reasons, many of the countries ceased to pay their quotas, a circumstance which made necessary a 40 per cent reduction in the budget of the Institute, with a consequent narrowing of its work.

In view of the fact that the government of Uruguay had endowed the Institute with an extraordinary allowance of $30,000 besides its annual quota, Miss Katharine F. Lenroot, United States delegate at the International Council of the Institute, suggested requesting from the other American states a similar extraordinary allowance; but nothing was done to that effect, since some of the countries had been unable to pay even their yearly quotas. The Institute's stability and broadening work requires the intellectual cooperation and economic contribution of all American countries, with the regular payment of their annual quotas, even if the amount of these has to be reduced in certain cases, as has been suggested by some states.

AUTHOR'S SUMMARY.

THE TEACHING OF CHILD CARE IN SCHOOLS AND WOMEN'S INSTITUTIONS. MARIA ANTONIETTA DE CASTRO, Bol. Inst. internac. am. de protec. a la infancia **7**:266 (Jan.) 1934.

Infant mortality in São Paulo decreased from 175.43 per thousand births in 1925 to 142.97 in 1932. This decline coincided with the hygienic measures taken by the Department of Inspection of Sanitary Education and Health Centers, which carried out an important campaign of prenatal and child hygiene.

The two chief causes of infant mortality are poverty and ignorance; to fight the latter all means of spreading the knowledge of child care should be sought. The teacher of health is entrusted with the task of divulging those facts in the dispensaries, schools and homes, as in São Paulo. In 1930, courses for "little mothers" had been organized in ten schools, with an attendance of 2,668 pupils; in 1933, the number of courses had increased to sixty.

The "Children's Crusade" was organized in 1930 and the "Child's Week" in 1931; the "Crusade" continued its work with 687 practical demonstrations, 21,659 consultations, 5,066 lectures, 6,274 visits to homes and 3,507 registrations of children, among whom 196,366 bottles of milk were distributed.

The Women's Professional Institute was the first to organize a dispensary for child care. It assisted 1,361 children at the Service for Child Hygiene and 153 at the Infants' Service, distributed 148,797 bottles of milk, provided individual instruction for 2,517 persons and 267 milk demonstrations and paid 407 visits to homes. The pupils, amounting to 503 in number, follow study and practical courses, the latter at the Dispensary, so as to form the "Health Flag": groups of 10 pupils of this association take under their care 5 babies and follow their development until they are 2 years old.

Study and practical courses of child hygiene are also given at the Domestic School of the Christian Women's League and at the Normal School of the Institute of Education.

The Health and Sanitary Education Service has organized courses for child care in fifty-nine groups of school children, with a registration of 4,058 girls between 12 and 15 years of age; the pupils of some schools have organized campaigns to fight infant mortality.

The problem of teaching child care in São Paulo is seriously dealt with in primary, normal, professional and domestic schools, in women's associations and in the dispensaries.

AUTHOR'S SUMMARY.

FIRST NATIONAL CONFERENCE ON DEPENDENT AND DELINQUENT CHILDREN: III. HOME COLONIES AND CONGREGATE-TYPE SCHOOLS. Bol. Inst. internac. am. de protec. a la infancia **7**:279 (Jan.) 1934.

The home is by far the best institution for the child's readjustment and education. When other establishments are necessary, those of a private character, with state supervision, control and financial aid, are the best. Experience of many years has led to disapproval of the type of congregate establishments and to preference for the family system or home colonies, under the direction of a married couple, in the belief that this is the best means of carrying out individual treatment adapted to each pupil's characteristics.

The Buenos Aires "Patronato Nacional de Menores" has adopted the system of country "family homes," which are provided with good means of transportation. Among the homes of this group is one dedicated to the newcomers, where each pupil is studied so as to permit a wise conclusion concerning his definite placement; there ought to be in addition another separate home for undisciplined children or for those who do not adapt themselves to family life.

The number of children in each home may amount to twenty-five or thirty, although the greater number is justified only by the necessity of reducing expenses. A new, cheaper system, allowing the "parents" to pay more attention to the pupils' education consists of a central kitchen and separate dining-rooms for all the "families"; these have lunch at their respective dining-rooms, breakfast and dinner being distributed by the central kitchen in the "homes."

The author is an advocate of the English "Borstal" schools and of naval schools on ships.

AUTHOR'S SUMMARY.

FETAL AND INFANT MORTALITY IN CATALONIA. AUGUST BROSSA ET AL, But. Soc. catalana de pediat. **3**:75 (April-June) 1930.

This article is an extensive survey of infant and fetal mortality. Individual discussions are given on the relation of syphilis, tuberculosis, mental diseases and abandonment of children to infant mortality. In Catalonia infant mortality dropped from 2.67 per thousand of population in 1920 to 1.87 in 1929. Study of the seasonal variation revealed that August and February showed high death rates. The leading causes of death in 1928 in Barcelona, the largest city, in infants from 1 month to 1 year of age, were: digestive disturbances (536), respiratory disorders (414), congenital debility (142), simple meningitis (139), tuberculosis (35), influenza (16), measles (11), grip 6), cerebral congestion (3), nephritis (3), diphtheria (2) and unclassified diseases (140).

WATSON, Elmhurst, Ill.

Society Transactions

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

Twelfth Annual Meeting, Brockville, Canada, June 1 and 2, 1934

H. P. WRIGHT, M.D., *President*

R. R. STRUTHERS, M.D., *Secretary*

First Session

Friday, June 1, 9 a. m.

TREATMENT OF ERYTHROBLASTOSIS OF THE NEW-BORN. DR. DOUGLAS P. ARNOLD, Buffalo, and DR. RICHARD A. DOWNEY (by invitation), Buffalo.

Universal edema of the new-born, icterus gravis and anemia of the new-born are considered from the point of view of differential diagnosis, prognosis and treatment.

The first is hopeless, both as to treatment and prognosis; the third is the least severe of all and with the proper therapy responds quickly and favorably.

Icterus gravis is considered in detail. The authors show that under early and specific treatment many children can be saved, even though suffering from a severe form of the disease. The diagnosis depends on rapidly progressive jaundice and anemia, usually with apathy, but sometimes with twitching and convulsions. The hemoglobin and red cell count drop rapidly; the bleeding time is prolonged; the results of the fragility test are not constant; hemorrhages may occur, the spleen and liver are enlarged, and there are usually, but not always, erythroblastosis and reticulocytosis accompanied by the appearance of immature leukocytes in the peripheral blood.

The differential diagnosis is then considered, taking into account physiologic jaundice, syphilis, congenital anomalies of the bile ducts, sepsis and hemorrhagic disease of the new-born. The authors emphasize the fact that properly performed, repeated intravenous transfusions of whole blood are the proper procedure. They have used this method of treatment for the last eight years and have had uniformly good results in cases in which the prognosis was poor. Blood given in any other manner is useless and inadequate. They also object to splenectomy, which they believe is unnecessary and results only in high mortality. They cite several cases in one family, with the normal children in the same family serving as a striking control series.

DISCUSSION

DR. H. P. WRIGHT, Montreal: Exactly what is meant by the term erythroblastosis?

DR. D. B. LEITCH, Edmonton: In a small series of patients whom I saw treated, when liver extract was given along with the intravenous transfusions, we were able to cut down the number of transfusions somewhat.

DR. H. P. WRIGHT, Montreal: How often did you give the extract?

DR. D. B. LEITCH, Edmonton: Every other day, alternating with transfusions, giving rather larger transfusions than ordinary—more than 200 cc. The results were apparently good, but the series was small.

DR. E. A. MORGAN, Toronto: In this series of cases was any late defect in mental or physical development noted?

Dr. Charles E. Snelling, Toronto: I think that Diamond, Blackfan and Baty, are in favor of repeated transfusions, though they do not emphasize it. In following the present series of cases I think that the members got the impression, whether it is the opinion of the writers or not, that the difference between erythroblastosis and the more severe grades of icterus gravis is very slight. May not a number of cases of icterus gravis in which cures are reported be only severe cases of anemia? In following a series we found a number of cases with nucleated cells. This condition persisted for two or three days, then disappeared. The one thing that must be kept in mind in icterus gravis is that nucleated cells are usually present. I should like to mention the case of one child whom we saw. This baby had shown anemia and became jaundiced. Two transfusions of blood—70 cc.—taken from the father were performed. Each time the child was all right for two days, then became worse. The suggestion was made that blood be taken from a different, unrelated donor. A nurse gave the blood, and from that time the child has been well.

Dr. Douglas P. Arnold, Buffalo: The term erythroblastotic anemia was originally used by Cooley in a slipshod way. Erythroblastosis in the new-born was described by him. In my opinion, the condition is absolutely unassociated with erythroblastic conditions in later life. I suggested another term, so that the condition might not become confused with hemolytic familial icterus and Cooley's anemia. I, too, have used liver for children with this condition. We had a number of cases in Buffalo a few years ago in which we used liver. The only reason that I did not speak of the liver is that the primary factor is repeated transfusions, and if one attempts other remedies, such as injections, the case is going to go by the board. I am sure that larger transfusions should be given. The amount depends on the hemoglobin. Dr. Morgan spoke of mental development in these patients. They seem to develop normally, except in long drawn out cases. As for physical development, they seem to do all right unless they get a severe infection of some kind. Dr. Snelling spoke of Diamond, Blackfan and Baty. I do not mean to criticize them, but I do not think that they emphasize the treatment enough, because just after they made their report a group of other investigators, particularly Cooley, in a round-table discussion, showed that they had not considered the results of that study, and I wanted to be sure to emphasize it. I think that there is enough clinical difference between severe physiologic icterus and so-called icterus gravis, and I tried to bring that out.

Bone Changes in Leukemia. Dr. Charles E. Snelling (by invitation), Toronto, and Dr. Alan Brown, Toronto.

Roentgenograms of children with leukemia have revealed changes in the structure of the long bones. These were observed by us independently, but a search of the literature shows that similar changes have been reported by a few authors. Our findings are recorded here.

The material for this report was obtained from roentgenograms and records of 12 patients with lymphatic leukemia studied in the Hospital for Sick Children, Toronto. Only those details of the laboratory and clinical findings by which the diagnosis was established will be given. They are recorded in the table.

Each of these 12 cases of leukemia at some stage showed bone changes. In case 8 there was only a rarefied area at the end of the bone; in case 4 there was periosteal elevation as well. These are all the patients with leukemia for whom we have roentgenograms of the bones in various stages of the disease. The age of all the patients of this series is below 6 years, and, for the most part, less than 4 years. The patients who showed periosteal elevation, as well as 2 of the other patients, complained of pains in the extremities. The symptoms of this group simulated those of rheumatic fever, and, in the 2 younger patients, scurvy and syphilitic bone change. The periosteal change might be confused with the picture of syphilitic disease of bone.

Allison, in 1924, reported a case of chloroma in a 3 year old girl, who showed raising of the periosteum that was similar to that in congenital syphilis. The

Laboratory and Clinical Findings in Twelve Children with Lymphatic Leukemia

Case	Age	Sex	History	Changes in Spleen	Changes in Glands	White Blood Cells	Lymphoid Cells, per Cent	Changes Seen at Biopsy Post Mortem	Roentgen Findings
1	2 yrs., 10 mos.	F	Pallor, tiring easily.....	+	+	2,000-20,000	84-90	+	Rarefaction at end of long bones adjacent to epiphyseal line
2	2 yrs., 6 mos.	M	Anemia, large abdomen...	+	+	33,000	88	+	Rarefaction at end of long bones adjacent to epiphyseal line
3	3 yrs., 6 mos.	M	Glandular enlargement ...	+	+	2,500-5,500	75-95	+	At first, normal; later, rarefaction of long bones adjacent to epiphyseal line
4	2 yrs.	M	Swelling in neck.....	+	+	300,000	99	+ ?	At first, normal; later, rarefaction of long bones adjacent to epiphyseal line
5	4 yrs.	F	Epistaxis	+	+	12,000-50,000	60-97	—	Normal on admission; later, rarefaction of long bones adjacent to epiphyseal line
6	3 yrs., 6 mos.	M	Pains in joints, swelling of joints, epistaxis	+	+	4,000-17,000	92-97	—	Normal on admission; later, rarefaction of long bones adjacent to epiphyseal line
7	3 yrs., 6 mos.	M	Weakness, fever, glandular swelling	+	+	1,900-6,500	95-100	—	Normal on admission; later, rarefaction of long bones adjacent to epiphyseal line
8	3 yrs., 6 mos.	M	Glandular swelling, pallor, pain in extremities	+	+	2,000-18,000	90-99	—	Normal on admission; later, rarefaction of long bones adjacent to epiphyseal line
9	6 yrs.	F	Fleeting pains in joints, fever, twitching of hands and face, pallor, irritability	+	+	3,500	98	+	Rarefaction at ends of bones, thinning of shaft, raising of periosteum
10	2 yrs., 6 mos.	M	Recurring pains in joints, pallor, swelling of parotid gland	+	+	1,400-14,000	15-90	++	Normal on admission; later, same changes as in case 9
11	6 mos.	M	Swelling of arms and legs, petechial hemorrhage	+	+	27,000-30,000	86-96	—	Generalized marked change as in case 9, plus spontaneous fracture of right femur
12	1 yr., 7 mos.	F	Pain and swelling of arms and legs	+	+	2,400-26,000	63-96	+	Marked changes, similar to those in case 9

new bone was laid down parallel to the shaft, except at the end, where it was at right angles. Taylor, in 1926, reported the case of a child of 2 years and 10 months with leukemia, who had pain and swelling of the extremities. Roentgenograms of the long bones showed elevation of the periosteum throughout. Karshner reported a similar case in a child of 2 years and 9 months. Karelitz reported one case of leukemia and one case of a patient with neuroblastoma who had periosteal elevation.

Poynton and Moncrieff reported 2 cases in patients who showed rarefaction at the ends of the long bones. Later, Poynton and Lightwood observed a patient who showed periosteal elevation.

The other diseases of the blood showing roentgen change in the long bones are: metastatic new growths with secondary anemia, marble bones, Gaucher's disease, chloroma, hemophilia and von Jaksch's or erythroblastic anemia.

Giles described the various types of nonsyphilitic periosteal lesions of bone, including fractures, following osteomyelitis, tuberculosis, typhoid fever, leprosy, pulmonary osteo-arthropathy, osteitis deformans, rickets, scurvy and bone tumors. He did not mention leukemia or chloroma.

Roentgen examination of the long bones is of value in confirming the diagnosis of leukemia. If a patient has a suggestive blood picture, examination of the bones may reveal the changes just described. Also, in conditions in which the patient has symptoms of rheumatic fever, examinations of the blood and the bones are necessary to rule out leukemia. Likewise, osteomyelitis has to be kept in mind in the differential diagnosis. One of the patients referred to in the bibliography was operated on for suspected osteomyelitis.

In summary, the roentgen changes in the long bones of 12 patients with lymphatic leukemia are described. In 8 they consisted of rarefaction across the shaft just adjacent to the epiphyseal line. In the remaining 4 cases there was also raising of the periosteum. Fleeting pains in the joints were noticed by 6 patients prior to admission. All the patients were less than 6 years of age.

BONE CHANGES IN LEUKEMIA: PATHOLOGIC FINDINGS. DR. I. H. ERB (by invitation), Toronto, and DR. ALAN BROWN, Toronto.

The changes in bone in acute leukemia in childhood may be grouped under the following headings: (1) infiltration, (2) rarefaction, (3) proliferation, (4) degeneration and (5) hemorrhage. These changes are illustrated in 2 cases of leukemia, one that of a girl who died at the age of 6 years, the other that of a boy who died at the age of 2½ years.

Infiltration by leukemic cells may occur in bone as it does in the liver and kidneys or elsewhere and may involve the marrow cavity, haversian canals or subperiosteal regions. By replacing bone marrow it may give rise to profound anemia. It is not visible in roentgenograms. Rarefaction occurs chiefly toward the ends of the long bones, but may occur anywhere along the shaft and involve both cancellous and compact bone. Proliferation of new bone occurs underneath the periosteum following stripping up of the periosteum by infiltrating leukemic cells. This new bone formation, as well as the areas of rarefaction, are demonstrable by roentgenograms. Degeneration of masses of leukemic cells, as well as hemorrhage into the marrow cavity, may occur in the course of the disease, but are of little clinical significance.

DISCUSSION OF TWO PRECEDING PAPERS

DR. SAUL USHER, Montreal: When the changes are seen in the roentgenogram, how do they compare with the onset of clinical changes?

DR. J. B. PRITCHARD, Montreal: Has Dr. Snelling ever found in the literature any report of osteosclerosis in leukemia? I saw a case of typical clinical leukemia in a child who had marked osteosclerosis of the bones of the knee and some of the ribs. The spleen was apparently not invaded, but marked hyperplasia was present. The femoral bone was extremely thick, but was not enlarged in circumference, and there were scarcely any marrow cells; the changes that Dr. Erb

saw were, I think, characteristic of bone tumors. Necrosis results from interference with the blood supply, and this suggests that in this condition there may be interference with blood supply, diminution of bone marrow, deposits of calcium and increase of bone toward the center of the shaft.

DR. ALTON GOLDBLOOM, Montreal: Is there any means of differentiating between bone changes in ordinary anemia and in leukemia? I ask this particularly because there are instances in which the blood picture of leukemia does not help one to know the extent of the changes. Has Dr. Snelling found distinctive differences between these two types of bone changes that would be a help in differentiating between the two conditions before there are typical changes in the blood stream?

DR. DONALD PATERSON, London, England: I should like to mention that at Great Ormond Street Hospital we are demonstrating the changes in the bones by the roentgen rays. I do not know whether we have worked up the pathology in the way that Dr. Erb has. I am particularly interested in Dr. Morgan's case, as I saw a similar case that we could not understand; now it appears that the condition may be a very early stage of leukemia.

DR. CHARLES E. SNELLING, Toronto: In reply to Dr. Usher's question as to how early the changes are seen, as compared with the onset of clinical changes, the boy of 2½ years, of whom I showed two roentgenograms, lived six and a half months. He died in December; the changes were apparent in September; the first roentgenogram we had was taken in July, but we were unable to arrive at a definite diagnosis of leukemia until we had a record of the pathologic findings. Throughout the course the blood count was always low; on two or three occasions the tension was 80 or 90 per cent. The majority of the lymphoid cells showed around 50 per cent—the normal distribution for a child. The 6 year old girl had been treated for rheumatic fever for some months by a local physician. She came to the hospital approximately one week before death, so we are unable to say how long before the change had occurred in that case. The reflection seen at the end of the bone does not occur at the onset of the changes. We have followed some of these children when they showed only slight clinical changes. In my searches of the literature I have found few cases of osteosclerosis with leukemia. We have, of course, searched only the surgical literature. Regarding Dr. Goldbloom's question as to bone changes in ordinary anemia and in leukemia, the conditions that we mentioned in the paper were specific conditions in which there were bone changes, with ordinary secondary anemia. I am not familiar with any bone changes in ordinary anemia; the changes seen in erythroblastic anemia are quite different.

The lines at the end of the bone do not occur in erythroblastic anemia. There is a more or less diffuse change of the whole structure, particularly in the small bones, in the new formation.

DR. I. H. ERB, Toronto: In reply to Dr. Pritchard's question, a short time ago I came across some references in the German literature to sclerosis associated with leukemia in adults. One should keep in mind that the disease is much more marked in adults than in children, and that it might be more possible for actual sclerosis to occur over a long period of time than it would during the short duration in children. Dr. Pritchard's suggestion that necrosis may perhaps be not necrosis but the cutting off of the blood supply concerned in the necrosis that is related to this sclerotic process seems a likely one, but as the leukemia cells in bone marrow disappear that space may subsequently be occupied by new bone and, given a longer period of time, the bone might become quite sclerotic. I myself have not seen this condition in any case.

SALT AND WATER METABOLISM IN A CHILD WITH ADDISON'S DISEASE. DR. H. B. CUSHING, Montreal.

A boy, 10 years of age, showing the classical symptoms of Addison's disease, died during an attack of extreme hypoglycemia; autopsy showed congenital absence of one suprarenal gland and marked hypoplasia and atrophy of the other.

During life the blood showed concentration due to dehydration, and a tendency to a low sodium chloride and sugar content.

Striking results followed the administration of sodium chloride in capsules; from 8 to 10 Gm. per day were required to maintain a normal water, sodium and chloride balance.

Observations in this case and in similar cases and recently published observations on suprarenalectomized dogs and cats indicate, first, that one of the main functions of the suprarenal cortex is to maintain the sodium and chloride balances of the organism and, through this, the water balance, and, second, that the loss of these balances leads to a definite clinical syndrome consisting of dehydration, hemoconcentration, circulatory collapse and sudden death (this syndrome being quickly relieved either by the use of suprarenal cortex extract or the administration of sodium chloride).

The authors suggest that a similar syndrome in the course of other diseases of childhood may be due to impaired function of the suprarenal cortex.

DISCUSSION

Dr. Douglas P. Arnold, Buffalo: I should like to ask Dr. Cushing how this child lived from the first to the tenth year without suprarenal cortex. I should like also to ask whether he has tried this treatment with sodium chloride in any toxic cases other than this. I have used calcium therapy in some younger infants with a toxic condition who went into collapse.

Dr. H. B. Cushing, Montreal: The length of time that the child survived surprised me, but I emphasized that he did not have total absence of the suprarenals; apparently he had enough to get along with that long, but evidently the gland failed when he reached a certain period of development. It occurred to me before, and particularly in connection with this boy, that possibly one has been emphasizing the amount of fluid rather than the sodium chloride. This patient was admitted to the hospital a short time before his final attack. He was at a boys' camp and was taken with an attack of vomiting and went into a condition of complete collapse. He was sent to the hospital in a state of collapse and vomiting. The condition was not recognized, and the pigmentation was attributed to solar rays. As he appeared dehydrated, he was given an intravenous injection of physiologic solution of sodium chloride containing dextrose. Somewhat unexpectedly, he immediately recovered, stopped vomiting, regained his appetite and seemed as well as ever, and did not remain in the hospital. On the second admission he again was brought in practically unconscious and was thought to be dying. Again, without a diagnosis being made, he was given an intravenous injection of dextrose solution, with the same spectacular result. The following day a diagnosis of Addison's disease was made. He was treated with capsules of sodium chloride, and, as I pointed out, the same result was obtained as by giving the sodium chloride intravenously.

Congenital Polycystic Disease of the Kidneys: A Report of Two Cases in One Family. Dr. Frank H. Boone, Hamilton.

Two children in the same family had polycystic disease of the kidneys. They died at 3 and 7 months of age, respectively. The observations at autopsy were given in one case. There was a strong history of kidney disease on the mother's side of the family. The physical and clinical findings and the observations at autopsy are discussed. Some of the literature with reference to the hereditary and familial character, types, frequency of the disease and pathogenesis is reviewed.

Von Gierke's Disease. Dr. Alan Ross (by invitation), Montreal, and Dr. Lionel M. Lindsay, Montreal.

Since 1929, when von Gierke first reported 2 cases of the syndrome which now bears his name, great interest has been shown in this disturbance of glycogen metabolism.

The clinical picture is that of a rather obese child usually undersized, with an unduly large abdomen, due entirely to an enormous liver. The size of the liver is caused by an abnormal accumulation of glycogen, which apparently can be mobilized only to a limited extent by natural means. Biopsy of tissue from the liver has shown its cells to be engorged with huge droplets of glycogen which almost fill the entire cell.

Examination of the blood shows a low sugar content and usually ketosis. The injection of epinephrine hydrochloride fails to produce the usual marked rise in blood sugar. The ketosis is usually increased. The cholesterol may be abnormally high. It would seem that although sufficient amylase is present in the liver and blood, it cannot, for some unknown reason, liberate dextrose.

Our patient was brought to the hospital at 27 months of age, because of a "big stomach." Physical examination revealed a pale baby with soft, flabby muscles and an unusual amount of fat deposited about the face. He was 4 inches (10.16 cm.) shorter than the average for his age. The abdomen was enormous, with a large firm smooth mass which we took to be liver. Rather extensive chemical studies of the blood showed: hypoglycemia (from 20 to 37); low sugar tolerance curves; a slight rise in the blood lactic acid, and acetonuria, after the injection of epinephrine hydrochloride; lipemia (0.753 per cent fatty acids), and a high cholesterol content (375 mg. per hundred cubic centimeters). We present this case as one of hepatomegaly possibly due to an upset glycogen metabolism similar to the cases described originally by von Gierke, possibly at an early stage of the disease.

DISCUSSION

Dr. Donald Paterson, London, England: I am not prepared with exact facts to contribute to a discussion of this paper, but some of the members will remember that at the meeting of the British Medical Association in London some years ago and, afterward, at the Third International Pediatrics Congress, Dr. Poynton presented some cases which he called familial. I think that there were 3 patients in one family and 4 in another, and they all had a large liver—so large that one could put the child on its back and push the liver almost up to the costal margin, and when one took one's hand away it fell back to the normal position. Credel published his paper about this case two or three months ago. Robert Ellis of Great Ormond Street Hospital undertook to investigate these cases and to report on them at the British Paediatric Association last month. I first investigated them in 1919; it is now fifteen years since they have been followed. One patient is now 17 years old. They maintain excellent health morally and mentally and seem in every way normal, except for the stocky body and large liver. The findings were in every way those that Dr. Ross has described. The patients had a high cholesterol content, so far as I remember, and a low blood sugar level. The report of these cases will probably be published in the near future. There is nothing that I can add, except that such patients live for years. The one whom I had to do with personally I had under observation for seventeen years.

Dr. R. R. MacGregor, Kingston: Is there any blood in the abdomen in these cases?

Dr. Alan Ross, Montreal: There was no blood in any of those that I reported.

Amyotonia Congenita: Report of a Case, with Complete Pathologic Study. Dr. M. J. Gill, Montreal, Dr. Wilbur Sprong (by invitation), Montreal, and Dr. Lionel M. Lindsay, Montreal.

A French-Canadian girl, aged 3 weeks, weighing 6½ pounds (2,948.34 Gm.) was admitted to the Children's Memorial Hospital on Aug. 11, 1933.

There had been paralysis from the neck down since birth. The mother observed on the day of birth that the baby did not move the arms or legs, and the condition had been the same since. Breathing was entirely abdominal. There had been diarrhea for several days.

The baby was born at full term of a seventh pregnancy and weighed 7 pounds and 9 ounces (3,430.28 Gm.). Birth was easy, by head presentation; no instruments were used. The patient was not breast fed and had never had cod liver oil or orange juice.

The mother, father and 4 other children were alive and well. Two children died, 1 at 8 days, of an unknown cause, and 1 at 41 days, of congenital paralysis similar to that in this case. This child was born of the fifth pregnancy. Birth was easy, by head presentation, and no instruments were used. Otherwise the family history was irrelevant. The Wassermann reaction of both the father's and the mother's blood was negative.

Physical examination showed a well nourished infant who did not appear ill. The head was normal in contour; the hair was abundant and extended down over the forehead to the eyebrows. The anterior and posterior fontanels were open. The nose, ears, mouth and the fundi oculi were normal. The chest did not move on respiration. Respirations which were paradoxical were rapid and entirely diaphragmatic. The ribs were deeply indrawn on inspiration. The chest was resonant throughout. The heart was normal. The abdomen was protuberant; there were jerky respiratory movements. The liver and spleen were palpable. There was a whitish vaginal discharge; a smear showed many gram-positive diplococci. All the extremities were flaccid; the baby lay with the forearm flexed on the upper part of the arm, the wrist being flexed on the forearm; there was complete wristdrop on both sides—evidence of contraction of the flexor group, as opposed to the extensors. The lower extremities showed flexion at the knees; the hips and feet were held in the position of equinus deformity.

Examination of the nervous system showed no abnormal signs referable to the cranial nerve, no palpable abnormality at the back of the pharynx and no palpable abnormality of the spine. No deep or superficial reflexes were obtained. There was some weakness of both triceps and both biceps and of the flexors and extensors of the fingers. Some weak movement was detected in all the muscles of the lower extremities except the tibialis anticus. The facial nerves responded only to galvanic current. Electrical responses were obtained only with galvanic current, and then only when the muscles were stimulated. There was no response to stimulation with galvanic current over nerve trunks. Electrical tests produced apparently little discomfort; there was little evidence of pain, even with strong faradic currents.

Lumbar puncture showed a pressure of 70 mm. of water. The Pandy reaction was negative. There were 3 cells. No lead was detected in the spinal fluid. The Wassermann reaction of the blood was negative.

Examination of the blood showed: 3,800,000 red cells, with 80 per cent hemoglobin, and 11,400 white cells. A differential count showed polymorphonuclears, 52 per cent; lymphocytes, 40 per cent; eosinophils, 2 per cent, and monocytes, 2 per cent. There was no stippling of red blood cells. The blood sugar was 94 mg. per hundred cubic centimeters; urea nitrogen, 28 mg.; uric acid, 3.4 mg.; phosphorus, 5.07 mg.; creatinine, 1.62 mg., and creatine, 1.06 mg.

The urine was normal.

Roentgenograms of the spinal column and chest were normal.

Investigation of the home conditions showed no lead plumbing. The father was a plumber; the mother had been in good health during the pregnancy up to the seventh month, when she strained herself by lifting; during the ninth month she contracted whooping cough; she stated that she had felt the fetal movements at the fourth month and thereafter up to confinement.

The child continued in the same condition; she retained sphincter control. Death occurred on October 15, with active respiratory infection and bronchopneumonia. We believe this case to be one of Oppenheim's disease.

Oppenheim's disease is a disease beginning at birth or in early infancy and is due to congenital developments; there is a defect of the lower motor neurons and of voluntary muscles. Clinically, it is characterized by weakness, hypotonia and quantitatively diminished electrical response in the muscles, without disturbance of sensation or mentality. The disease was first described by Oppenheim in 1900

and was called myatonia. This name, because of its similarity to myotonia (Thomsen's disease), was changed to amyotonia at the suggestion of English physicians. The disease is classified under many names in the literature.

In 1917, when Faber reviewed the literature on Oppenheim's disease, 115 cases had been reported; 3 were of familial occurrence. In 1923, 125 cases were reported and since then, 15 more have been recorded. From 8 to 10 cases were of familial occurrence. In 1930, Forbes and Wolf of Johns Hopkins Hospital reported amyotonia in identical twins.

There is a growing recognition of two forms of amyotonia congenita, the more common being that which occurs in one member of a family and which is malignant; the patient dies in early infancy. The other form, which is about one tenth as common, is familial and relatively benign and may escape diagnosis until the patient reaches puberty; he may practically recover.

Syphilis and other infections play no part in the etiology; in only 1 case that was reported was there a positive Wassermann reaction of the blood; a positive tuberculin reaction was never found. The earlier investigators stated that heredity plays no part, but statistical study does not justify such an inference. The fact that quickening was absent, weak or retarded in 54 per cent of the cases reported up to 1927 and normal in only 5.4 per cent proves clinically that the disease is present before birth. Pregnancies, with 2 exceptions among 125 cases, ran a normal course to birth at full term, indicating that incidents of gestation are not important in producing the disease. Toxins involving the neuromuscular system cause these symptoms; in some cases the condition occurs postnatally after an acute infection; the toxic theory can explain the amelioration that often occurs in these patients.

In the 8 to 10 instances of familial occurrence, study of the patients suggests the possibility that reproductive exhaustion may be a factor in producing the disease. In 63 per cent of the cases reported the patient was born of a fifth or later pregnancy.

The most prominent symptom is bilateral muscle flaccidity affecting all the extremities and probably all the muscles of the trunk, including the intercostal muscles. Hypermotility of the joints is a constant symptom in from 90 to 95 per cent of the cases; weakness or paralysis was noted at birth in 81 per cent. Fifty-three per cent of the patients were males; 47 per cent, females. The muscles of deglutition, mastication and of the diaphragm were spared, showing that muscles innervated by cranial nerves are rarely involved. Nystagmus was present in 3 cases, strabismus in 4 and ptosis in 2. The prevalence of symptoms in the lower extremities rather than in the muscles of the upper part of the body suggests the possibility of a progressive ascending type of paralysis. The tendon reflexes were absent in approximately 75 per cent of the cases, diminished in 20 per cent and normal in 2 per cent. The superficial reflexes were normal in from 40 to 50 per cent. Sphincter control was usually normal. Sensation was normal in from 85 to 90 per cent.

Improvement was generally noted in from 50 to 90 per cent of the cases; no report of complete recovery was found in the literature.

DISCUSSION

Dr. Donald Paterson, London, England: May I ask Dr. Gill and Dr. Sprong their advice on the relationship of the disease that they have described to Weigert-Hoffman disease. Are these the same disease, or are they two different diseases, and is the spreading of the diaphragm described clinically seen? In 6 of the cases reported and in some patients whom I examined at Great Ormond Street Hospital the diaphragm has always been the center. At the National Hospital they seem to hold the opinion that these two conditions are the same disease.

Dr. Wilbur Sprong, Montreal: I have no personal opinion to offer. A contribution along this line that was published in Bern in 1927, I think, contained a mass of evidence that no one else has brought forward so far in defense of the thesis that the two diseases are the same. It was, however, brought out in a

discussion by certain clinicians that the Weigert type of amyotonia is distinctly different clinically, in the first place, in that amyotonia congenita shows improvement and exists for a long time, whereas it seems the consensus of experience that in Weigert-Hoffman's disease there is progressive muscular disorder; the child never appears well or happy, but is recognized at once as being ill, and usually dies within a few years.

Second Session

Saturday, June 2, 9 a. m.

RELATIONSHIP OF SEDIMENTATION RATE TO ALTERATION IN THE ALBUMIN-GLOBULIN RATIO IN RHEUMATIC INFECTION IN CHILDHOOD. DR. R. R. STRUTHERS, Montreal, and DR. H. L. BACAL (by invitation), Montreal.

Our observations concern the alteration in the albumin-globulin ratios in the blood protein, which we have found to be consistently altered in the presence of alteration of the sedimentation rate.

In a rather extensive study of the clinical value of the estimation of the protein fractions in the blood plasma, Johansen found the albumin-globulin ratio altered by various diseased conditions in a manner corresponding strikingly to the alteration in the sedimentation rate. Repeated examinations showed that an increased sedimentation rate is associated with an increase in the fibrinogen and euglobulin fraction of the plasma. Only in cases of marked reduction in the number of red cells or in hydremia did he obtain conflicting values.

In chorea uncomplicated by carditis, in which the sedimentation rate is consistently normal, there is no noteworthy alteration in the albumin-globulin ratio, as one would expect. In acute rheumatic fever, in which the sedimentation rate is high, there tends to be a marked alteration in the ratio, in that the albumin is decreased and the globulin increased, with some lowering of the total protein values.

In acute rheumatic fever or chorea, with complicating carditis, in which the sedimentation rate is increased, there is a marked alteration in the albumin-globulin ratio; in fact, this ratio may be so altered as to be inverted, as one is accustomed to find in nephritis. During the course of the subsidence of the disease, however, these values tend to return to normal. In the presence of cardiac failure with edema, in which the sedimentation rate falls to levels below the normal, this reversal may or may not hold true. The reason for this inconsistency is not apparent.

The following conclusions may be drawn:

Alteration in the sedimentation rate which has been shown to occur in association with rheumatic infection in childhood is associated with definite alterations in the albumin-globulin ratio, in that there are a drop in the concentration of albumin, a rise in the concentration of globulin and some diminution in the total protein of the blood.

CLINICAL COMPARISON OF THE VALUE OF VARIOUS ANTIRACHITIC SUBSTANCES. DR. T. G. H. DRAKE, Toronto, DR. F. F. TISDALL, Toronto, and DR. ALAN BROWN, Toronto.

At the present time roentgen examination is the best means of diagnosing rickets, and reliance cannot be placed on the usually accepted clinical signs, namely, craniotabes, rosary or moderate enlargement of epiphyses. Toronto sunshine as at present used is not entirely efficacious in preventing roentgen evidence of rickets. Infants under 4 months of age in October are more apt to have rickets in the succeeding five months than are infants from 4 to 8 months of age in October. One or 2 teaspoonfuls of cod liver oil were as efficacious as 3 teaspoonfuls in preventing the development of rickets. One hundred, 200, 400 and 800 units (from 2 to 11 drops) of viosterol were efficacious to the same degree in preventing rickets. Irradiated vitamin D milk is a valuable addition to the present rickets-preventing armamentarium.

DISCUSSION

Dr. Douglas P. Arnold, Buffalo: I should like to know whether physicians are going to abandon cod liver oil in favor of viosterol and irradiated milk.

Dr. George Smith, Toronto: I should like to know how thoroughly the babies were exposed to suntan before the experiment.

Dr. F. F. Tisdall, Toronto: Some significant facts were presented by Dr. Drake. But a word of caution ought to be spoken here. Dr. Drake has presented results the evidence for which is based on a small series of cases. It is true that 100 or 200 units of viosterol has prevented roentgen evidence of rickets just as effectually as 800 units. However, so little is known about the deposition of lime salts in bone that one should still keep in mind that it is not proved at all yet that 100 units of viosterol is just as effective and beneficial as 800. It does prevent the evidence of rickets as well, but it is possible that the deposits in the ends of the bones are not as good as with the larger doses. The practical conclusion from the standpoint of the question of irradiated milk is that in the case of a small infant, one under 4 or 5 months of age, although irradiated milk furnishes vitamin D, it does not entirely benefit in all cases. Its great benefit would lie in the fact that it furnishes vitamin D in additional doses, as we are giving it, in cases in which there is difficulty in administering cod liver oil.

Dr. Alton Goldbloom, Montreal: Dr. Drake did not refer to phosphorus in the blood stream. I wonder whether he has made any study of this.

Dr. George Campbell, Ottawa: What is the additional cost of viosterol treatment?

Dr. H. P. Wright, Montreal: I should like to say that at the meeting of the International Association of Preventive Pediatrics Dr. A. F. Hess read an interesting paper along somewhat similar lines. He has died since then. The question of the study of rickets is now a very important one, and I am sure that it is the hope of all the members present that Dr. Drake will continue to make studies and present the results from year to year.

Dr. T. G. H. Drake, Toronto: Dr. Tisdall has practically answered Dr. Arnold's question. In reply to Dr. Smith as to the thoroughness of the exposure of these babies to sunshine, the children were under the control of the Toronto Well Babies' Clinics, and the amount of exposure to sunshine was that which is ordinarily supplied at these clinics. With regard to studying the phosphates, it was absolutely impossible with these babies. They were from the Well Baby Clinic, and the mothers objected so much to our working on them that it was impossible to do blood tests. With regard to the additional cost of irradiated milk, there is no irradiated milk being produced commercially at present. The extra cost ranges around 1 cent per quart.

Sensitivity to Tobacco in Children. Dr. Alton Goldbloom, Montreal.

Six cases are presented in which various manifestations of sensitivity were found to be due to tobacco. In one child who complained of asthmatic attacks sensitivity to orris root was first established, and later, when he returned with a recurrence of attacks in spite of no exposure to orris root, tobacco was found to be the offending atopen. The second patient, who was first found to be sensitive to dog hair, was later, on the recurrence of symptoms, found to be sensitive to tobacco. A third child was polysensitive, particularly to fish. He was found to be sensitive to tobacco, together with numerous other substances. Two children, aged 9 and 11 years, respectively, had had asthmatic attacks since about the age of 3 months. Numerous skin tests had been made on both children in attempts to discover the cause. In neither child had tobacco ever been tried. The finding of tobacco as the exciting agent and subsequent desensitization made possible a final cure in each case.

The final case reported was that of a child who had cerebral angioneurotic edema with facial paralysis, semicoma and vomiting. Several diagnoses, such as

poliomyelitis, encephalitis and lead poisoning, were made. After several months unmistakable evidence of angioneurotic edema was found in the form of recurrent edema of the upper and lower eyelid and of Tenon's capsule of the left eye. With this as a lead, a vigorous search for atopens was made; the patient reacted moderately to feathers and wheat and markedly to tobacco. In this case, also, desensitization caused the disappearance of all the symptoms.

In obtaining the history in several of these cases, it was evident that the children were better and sometimes symptom-free when they were away from their fathers. Such evidence should offer an important lead in establishing a causative agent for allergic symptoms.

DISCUSSION

DR. GEORGE CAMPBELL, Ottawa: When I received the program for this meeting I had our records looked up and found that within the last fifteen years we have tested some 400 or 500 children suffering from colds and other conditions for sensitivity to tobacco. One case in particular is worth mentioning: that of a mother who was a cigaret smoker who did not wash her hands before she put her child to the breast. I wish to ask Dr. Goldbloom what solution of tobacco he began with in treating these patients.

DR. H. L. BACAL, Montreal: One hundred cubic centimeters diluted in 40,000 was used. We made intradermal tests first to determine how sensitive the child might be and with what solution we might begin. Some solutions are stronger than others. Sometimes one can give only a 1: 100,000 solution, and sometimes even smaller dilutions must be used in beginning treatment.

ABSORPTION AND UTILIZATION OF IRON. DR. PEARL SUMMERFELDT, Toronto.

From the experiments that have been done on animals by feeding α-α-dipyradil, which reacts only with ferrous chloride, one may conclude that salts with organic iron would have to be reduced to a ferrous state before the iron could be absorbed and utilized for the production of hemoglobin.

In experiments on animals there is a greater response to ferrous chloride than to other iron salts when they are fed with equivalent amounts of iron. Organic iron, when fed in the same amount, does not produce the same response in hemoglobin.

Experiments were carried out to determine the amount of iron that would be available for absorption after gastric digestion. These were done in vitro with pepsin and tenth normal solution of hydrochloric acid.

The following results were observed:

1. Vegetables and fruits have a relatively low total iron content, but after gastric digestion from 40 to 84 per cent of their total iron was available for absorption or was present in a soluble state. Spinach was an exception, as only 20 per cent of the total iron was made available. In the gastric digestion of meats and eggs very little iron was made available for absorption.

2. When vegetables and fruits were cooked, a higher percentage of iron was made available.

3. In comparing the available iron in water in which vegetables had been cooked with the total iron content, it was found that about 100 per cent of the iron in such water is in a soluble state. Furthermore, from 24 to 54 per cent of available iron of the cooked vegetable is lost if the water in which the vegetable has been cooked is discarded.

DISCUSSION

DR. F. F. TISDALL, Toronto: One surprising fact that I noted was the small amount of iron in egg yolk which is available. Is this Dr. Summerfeldt's experience in feeding animals egg yolk? Has she found that egg yolk is of value in increasing the iron content of the blood of rats?

DR. GEORGE SMITH, Toronto: I had the opportunity of following on the ward the cases that Dr. Summerfeldt reported. The cure was remarkable to all of us, and I have never seen similar cases of anemia in which recovery was so prompt. With regard to the ferrous chloride, I wonder how much was left in the fluid after preparation and what it had to do with the action. I also gave iron to a patient, without results, but then added hypochloride solution, with active results. I have no doubt that it is a wonderful thing for anemia.

DR. DONALD PATERSON, London, England: I should like to ask about the practical application of ferrous salt. How does Dr. Summerfeldt prescribe it for a patient; how would she write a prescription?

DR. SAUL USHER, Montreal: I have seen ferric chloride or phosphate given to a great number of children without the addition of copper, without any change, but found a great change on treating them with the addition of copper.

DR. PEARL SUMMERFELDT, Toronto: In reply to Dr. Tisdall, we found no response in hemoglobin even on giving the rat as much as half an egg daily. In reply to Dr. Smith, there is some free ferrous acid, but I do not know how much. I have not written a prescription for the ferrous salt, as we prepared the ferrous chloride in the laboratory.

MENINGOCOCCIC MENINGITIS. DR. ALAN BROWN, Toronto, and DR. NELLES SILVERTHORNE (by invitation), Toronto.

This report embodies a review of three years' study of meningococcic infection and is summarized in lantern slides. The plan of study is outlined. An analysis of the clinical material is made, with reference to the bacteriologic findings and an epidemiologic survey of carriers and cases. A correlation is shown between the incidence of carriers and colds in a group of 50 normal noncontacts (laboratory workers) and the occurrence of sporadic cases of the disease. The geographic distribution of cases of meningitis occurring in Toronto is presented. In conclusion, an outline is given of the pathway of dissemination of the meningococcus, e. g., by a chronic carrier or a temporary carrier, and the rise in the carrier rate at times of epidemic coryza and its relation to sporadic and epidemic occurrence of the disease are discussed.

DISCUSSION

DR. H. P. WRIGHT, Montreal: Is it usual to have only two epidemics of respiratory infection a year in Toronto? The Germans speak of a catarrhal infection once a year. The normal person usually has more than one or two a year. The condition should be investigated. Some years ago at the Foundling Institute we found an incidence of three a year, one in September, one at Christmas and one in the spring. I bring this question up because the time of year does seem to be associated with respiratory diseases.

DR. DONALD PATERSON, London, England: I was interested to note the large number of cases in which a diagnosis was made. It has been my experience, as well as that of many of my associates, that meningococcic meningitis is an extremely difficult disease to diagnose in the early stages in very tiny infants. Dr. Silverthorne passed over that point rather rapidly. It is the sort of condition that one could have in a ward and see for three or four days and never suspect cerebral symptoms. At least, that has been my experience.

DR. NELLES SILVERTHORNE, Toronto: In answer to Dr. Wright, it is difficult, of course, and only a matter of judging a small group of fairly normal persons to state definitely whether they have colds in the head more than twice a year. The opportunities of noticing it at those times were better, as there was an epidemic of colds in the laboratory, and persons were getting them one after the other. In answer to Dr. Paterson, I think that all pediatricians appreciate the difficulty of diagnosing this condition in infants, and the only possible way to be on the safe side is to suspect the condition in any child with an unexplained fever. Many of them have been found by blood tests to give definite bacterial cultures.

EFFECT OF VARIOUS DEFICIENT DIETS ON THE RATE OF LEARNING OF RATS. DR. KARL S. BERNHARDT (by invitation), Toronto, and DR. F. F. TISDALL, Toronto.

These investigations were carried on as a cooperative project by the department of pediatrics and the department of psychology of the University of Toronto. The object was to test the effect on the learning ability of various deficient diets, namely, a diet deficient in phosphorus and a diet deficient in protein.

The vitamin B deficiency in diet occurred during the first 4 weeks of the life of the rats and was administered through the diet of the mothers of the litters during the nursing period. The other dietary deficiencies occurred after the rats were 4 weeks of age and lasted throughout the entire period of the learning tests.

The learning tests consisted of a water maze and a multiple choice apparatus. The motivation used was escape from water. The rats were required to learn the water maze, relearn the same maze two months after completing learning and learn a simple multiple choice problem in the water tank. The learning scores of the different groups on a deficient diet were compared with those of a control group on a normal diet.

On all measures of learning the maze, relearning the maze and learning the multiple choice problem the group which had been deprived of vitamin B during the nursing period had poorer average scores than the normal control group. So vitamin B deficiency during the first few weeks of the life of the rat has an adverse effect on the learning ability of some animals, even though it is given in abundance during the time of the learning tests. Vitamin A deficiency during the time of the learning tests, although serious enough to cause most of the group to die before the end of the experiment, did not reduce the learning ability of the rat. Phosphorus deficiency reduced the learning scores considerably. Protein deficiency was even more effective in reducing the learning ability of the rats on that diet.

DISCUSSION

DR. H. P. WRIGHT, Montreal: Were any observations made on the stools of these rats? Was there constipation?

DR. F. F. TISDALL, Toronto: So far as the vitamin B deficiency is concerned, one puts them on a deficient diet and feeds them carbon; marked stasis is immediately evident.

DR. GEORGE SMITH, Toronto: Did they tend to become normal after being put back on a normal diet?

DR. D. B. LEITCH, Edmonton: Was any particular type of protein used, or did the rats do better on a special animal type?

DR. KARL S. BERNHARDT, Toronto: The deficiency was, of course, during the time of nursing. After that the animals were fed a normal diet containing animal vitamin B. We made no tests of any of the carbons. As for the matter of retesting these animals, after they had been tested, while they were on a deficiency diet they were retested, and after that they were put back on a normal diet. The experiment presents many difficulties from a standpoint of testing procedure. We had to devise a number of new learning tests because we could not give them the same tests again. As for the form of protein, up to the present our work has been exploratory, and we have tried various kinds. The field is new; there have been few experiments, and a great deal remains to be done. This would be a good field for research.

CONGENITAL CYST OF THE LIVER. DR. JOHN L. MCDONALD (by invitation), Toronto, and DR. ALAN BROWN, Toronto.

A 10 month old infant became suddenly ill two days before admission to the hospital, with vomiting and slight abdominal distention. All food was discontinued, and sugar solution only was administered. When seen and examined twenty-four hours later, the infant appeared comparatively normal. There was no toxemia, and

the child seemed happy, but the abdomen was full. An indefinite mass was detected on the right side of the abdomen, but nothing was felt by rectum. A diagnosis of incomplete obstruction was made, and laparotomy was advised.

On examining the child with the fluorescent screen before operation, there seemed to be a dense opacity involving most of the right side of the abdomen and, to a slight extent, the left side from the diaphragm to the pelvis. The descending sigmoid flexure and the rectum were filled with gas and were visible.

At operation exploration revealed the liver to be greatly increased in size in the anteroposterior as well as the lateral diameter. The external surface was smooth and the free margin sharp, but rather abruptly rounded off into a large mass, the external surface of which was covered by liver substance. Fluctuation could be detected, and on aspiration 20 cc. of straw-colored fluid was obtained. The child died two days later, apparently from shock following operation. A section of liver from the edge of the cyst showed it to be lined by loose myxomatous tissue; the bulk of the parenchyma of the liver had been destroyed, and only a few atrophied liver cells remained. Much fibrous tissue could be seen; the greater part of this probably represented the original stroma of the liver after the liver cells had disappeared.

DISCUSSION

Dr. Donald Paterson, London, England: I have never seen a case like this. I am the curator of the museum at Great Ormond Street Hospital for Sick Children, and, so far as I am aware, there is no similar specimen in our collection.

A Case of Persistent Pyuria Healed by Presacral Sympathectomy. Dr. Pearl Summerfeldt, Toronto, and Dr. Alan Brown, Toronto.

A child 13½ months of age had a history of persistent pyuria of more than six months' duration. On admission the urine contained albumin, from 20 to 40 white blood cells per high power field and some clumps. The culture of the urine grew Bacillus coli-communis.

On investigating the case neuromuscular dysfunction of the left side was found, with a moderately large bladder and with hydrocele and hydronephrosis on the left. In this type of case there is imbalance between the parasympathetic and sympathetic nervous system, the sympathetic nervous system being overactive. Retention of urine in the bladder and left urinary tract was produced in this child. Following this, passive congestion of the kidney occurred, which lowered the resistance of the kidney to any organism that might be present. Presacral sympathectomy was performed. The capacity of the bladder was definitely decreased at the end of a month, and though the size of the lower half of the left ureter was about the same, the upper half had decreased about one half of its original size.

On the patient's discharge from the hospital the urinary infection had not entirely cleared up, as there were still 1 or 2 pus cells in the urine and a faint trace of albumin. The urine still contained numerous organisms.

DISCUSSION

Dr. Fred Shippam, Montreal: Regarding the treatment by sympathectomy, I saw 2 or 3 patients who were operated on in this way at Birmingham, England, during the past twelve months. None showed any improvement. I noticed in following the series of pyelograms that the first series were those in which the dye was introduced by means of a ureteral catheter, in which case the ureters showed great dilatation according to the pressure used in introducing the dye, whereas the final roentgen picture was that in which intravenous pyelography was used and, as usual, the shadow was less distinct and smaller. This would give a misleading finding. The same method of introducing the dye should have been used in taking all the roentgenograms to avoid misinterpretation.

Dr. Alan Ross, Montreal: Was there any evidence of anatomic narrowing at the mouth of the bladder?

DR. PEARL SUMMERFELDT, Toronto: When the dye is introduced by means of a cystoscope the shadow is usually better, but the intravenous method is said to give a true shadow. There was no narrowing at the mouth of the bladder.

EFFECT OF IMMUNE GLOBULIN (PLACENTA) ON THE DICK TEST: PRELIMINARY REPORT. DR. ALAN ROSS (by invitation), Montreal, and DR. H. B. CUSHING, Montreal.

Recently McKhann and Chu of the department of pediatrics of Harvard University Medical School succeeded in extracting from the human placenta a protein fraction that has definitely been shown to: (1) neutralize diphtheria toxin, (2) blanch scarlet fever rashes, (3) neutralize the poliomyelitis virus and (4) prevent measles in exposed susceptible patients.

As little in connection with this protein fraction has appeared in clinical journals and as the material will probably soon be available and in general use, we thought that it might be appropriate to review briefly the literature on the subject, especially the work of McKhann, and to present the preliminaries of work which we have undertaken in connection with the Dick test.

A study of the age at incidence of infectious disease reveals the fact that for some time, usually for months, new-born infants appear to be immune to measles, scarlet fever, diphtheria, poliomyelitis and mumps. There are three possible routes by which this immunity may reach the infant: (1) by the colostrum or milk of the mother, (2) actively or passively through the placenta and (3) by immune properties possessed by rapidly growing tissue.

(To be concluded)

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Dec. 18, 1934

STANLEY GIBSON, M.D., *President, Presiding*

REPORT OF CASES: CEVITAMIC ACID (ASCORBIC ACID) IN THE TREATMENT OF INFANTILE SCURVY. DR. ARTHUR F. ABT and DR. ISADORE EPSTEIN.

The isolation of a vitamin in crystalline form not only is a matter of theoretical importance, but such a discovery also has possibilities in practical clinical application. In 1928, Szent Györgi isolated a chemical which he thought was hexuronic acid and which he believed to be identical with vitamin C. Well controlled experiments on laboratory animals with this substance demonstrated that it protected against scurvy and cured this disease when experimentally produced. In 1933, the name of the isolated acid was changed to ascorbic acid as its chemical formula became better known and it was found not to be hexuronic acid. More recently the Council on Pharmacy and Chemistry of the American Medical Association designated cevitamic acid as the approved nonproprietary name for this substance.

Cevitamic acid is a white or slightly yellow-white, odorless crystalline powder, the chemical formula of which is $C_6H_8O_6$. Cevitamic acid may be isolated from vegetable and animal sources. The product with which we were supplied was isolated from vegetable sources. The tablets which were used contain 10 mg. of the acid compounded with milk sugar and are for oral use. They are best given dissolved in from 10 to 20 cc. of water or milk. It is said that 10 mg. of crystalline cevitamic acid corresponds to approximately 30 cc. of the active vitamin C in fresh orange juice.

This paper reports the treatment of 3 infants with clinical scurvy by the oral administration of cevitamic acid tablets. The first patient was an 11 month old boy, whose case we report with the permission of Dr. Edward W. Beasley. The infant had been fed an evaporated milk formula with no orange juice and showed

typical clinical symptoms and signs, as well as roentgen findings, of scurvy. Attempts to administer orange juice were unsuccessful because of emesis. Three 10 mg. cevitamic acid tablets were given orally daily and were successfully retained. Clinical improvement was noted in forty-eight hours. Roentgen examination one month later showed calcification of the subperiosteal hemorrhages.

The second and third cases reported were those of infants treated with the permission of Dr. Joseph Brennemann at the Children's Memorial Hospital. The second case was that of a 1 year old girl with a clinical history, symptoms and signs of scurvy. Two 10 mg. cevitamic acid tablets were given orally for the first four days, after which four tablets were given daily for ten days. Clinical improvement was definite after twenty-four hours.

The third case was that of a 9 month old infant with a definite history, symptoms and signs of scurvy. She was given treatment similar to that given the second patient. Definite improvement was noted after forty-eight hours.

Besides being able to report the efficacy of cevitamic acid in the treatment of these three patients with infantile scurvy, we were enabled, in the last two cases, to determine the cevitamic acid content of the blood serum, both before and after treatment. So far as we know, no such determinations have been previously reported in infantile or adult human scurvy.

The determinations of the cevitamic acid content of the blood serum were made by Dr. Studeville in Dr. Farmer's laboratory of biologic chemistry at the Northwestern University Medical School. The method used for the test was that described by Tillman and was based on the modifications of Harris and Ray.

In the second case the blood serum was found to contain 0.97 mg. of cevitamic acid per hundred cubic centimeters before treatment was instituted; this had increased to 2.01 mg. after six days of treatment. In the third case the blood serum content of cevitamic acid was 1.02 mg. per hundred cubic centimeters before treatment, and it had risen to 2.08 mg. after six days of treatment. These results should be taken as comparative rather than absolute values.

It may be concluded that in the 3 infants presented the oral administration of cevitamic acid seemed to effectively cure infantile scurvy. The doses used were from 20 to 40 mg. daily, given orally for from one to three weeks.

This method of treatment seems to be of especial value in such cases of infantile scurvy as the first case here reported, in which the infant failed to retain the orange juice offered as treatment. In such cases, in which severe nausea and emesis make the retention of the usual vitamin C-containing fruit and vegetable juices difficult or impossible, smaller amounts of cevitamic acid in solution may be retained when given orally and effect a rapid cure.

The cevitamic acid content of the blood serum appears to be extremely low in infantile scurvy and is definitely increased after treatment with cevitamic acid.

AGE AND SEASONAL INCIDENCE IN THE MORBIDITY AND MORTALITY OF 20,000 INFANTS IN THE FIRST NINE MONTHS OF LIFE. DR. CLIFFORD G. GRULEE, DR. HEYWORTH N. SANFORD, DR. HARRY SCHWARTZ and DR. J. KANTOR AMTMAN (by invitation).

Charts are shown giving the age and seasonal incidence in the morbidity and mortality of 20,000 infants in the first nine months of life. These infants were segregated into three groups: those artificially fed, those partially breast fed and those entirely breast fed.

Two points are emphasized in these charts: First, there is an increased morbidity in the artificially fed child after the first six months of life. Second, there is an increased mortality in the artificially fed child throughout the first nine months of life. This is most marked in the first five months, when it is due to gastro-intestinal disturbance or miscellaneous infection.

It seems likely that this increased tendency to infection in the artificially fed child after the first five months of life may be attributed in all probability to the difference in the type of feeding. The child carries over with it from intra-uterine life a certain amount of protection against infection, and this protection lasts for

the first five to six months. It would seem that for some reason breast feeding tends to prolong that period of protection.

DISCUSSION

DR. ARTHUR F. ABT: In studying the charts showing the morbidity, which Dr. Sanford presented, I was reminded of the work of Dr. Helen Mackay of London, who studied the difference in hemoglobin and red blood cell values in breast fed and artificially fed infants. As I remember, her figures were approximately the same until about the fifth month of life. Thereafter the breast fed infants seemed to show continuously higher hemoglobin and red cell values.

I wonder whether the relative anemia of artificially fed infants, as compared with breast fed infants, would in some way explain the higher morbidity for the artificially fed infants after the fifth month. Of course, the curves for mortality which Dr. Sanford has shown need not be influenced by the relatively greater anemia of the artificially fed infants as compared with the breast fed infants.

DR. HEYWORTH N. SANFORD: One certainly should take into consideration what Dr. Abt has said, but when these studies were carried on, from 1926 to 1931, we were not considering anemia as much as we are now.

The one point against anemia being a factor is that there is little difference in the morbidity of the groups with respiratory disorders. The three groups were not far apart from the standpoint of morbidity. If anemia had anything to do with this, one would think the breast fed infants would have a much lower morbidity, but whether one can assume that or not I do not know.

ACUTE APPENDICITIS IN JUVENILE DIABETES MELLITUS. DR. ALVAH L. NEWCOMB.

In a group of 65 children with diabetes mellitus we saw 2 puzzling cases of abdominal pain evidently due to ketosis and 4 cases of acute appendicitis, one with accompanying ketosis, and 1 case of suspected appendicitis with a fecalith. The 2 cases of abdominal pain due to ketosis were characterized by persistent vomiting after an apparent dietary indiscretion, a distended abdomen, generalized tenderness with glycosuria and definite ketosis. A summary of these 2 cases follows:

E. H., a 12½ year old girl, with a history of diabetes of five years' standing, was seen in the home on July 1, 1932. She was under the supervision of a practical nurse while the mother was having a two weeks' vacation. The care was good for the first week and less good during the second week. The day preceding the illness the girl had gone bathing, then to a ball game and finally to a picnic where she had eaten potato salad. On reaching home she began to vomit and complained of fatigue and drowsiness, then abdominal pain. She vomited throughout the night. The following morning there was a slight odor of acetone to the breath, and sugar and diacetic acid were found in a specimen of urine taken about 8:00 a. m. There was some abdominal distention with generalized tenderness but no muscular rigidity. As the vomiting persisted, the child was admitted to the hospital. The blood sugar was 350 mg. per hundred cubic centimeters, and the carbon dioxide-combining power of the plasma was 18 volumes. The temperature was 100 F. She recovered promptly following the subcutaneous administration of insulin, dextrose and physiologic solution of sodium chloride.

D. B., a 4½ year old girl, was seen for the first time in the outpatient department of the Children's Memorial Hospital on June 10, 1934, where the following history was elicited:

She had had abdominal pain for eleven hours, vomiting for nine hours, deep, heavy breathing for seven hours, fever for six hours and backache for two hours. She had eaten canned salmon and pickled pigs' feet four hours before the onset of these symptoms. She was semicomatose; the pupils were widely dilated; there was an anxious facial expression. The abdomen, especially the lower half, was markedly distended, with tenderness, which was a little more marked on the left. The superficial veins of the abdomen were engorged. The temperature was 100 F., and the total leukocyte count was 34,750.

A tentative diagnosis of acidosis due to food poisoning, of peritonitis or of early pneumonia was considered. A urine heavily loaded with sugar and acetone bodies established the diagnosis of diabetes ketosis, which was substantiated by the disappearance of the abdominal symptoms, the glycosuria and the ketonuria after the subcutaneous administration of fluids and insulin.

In the 4 cases of appendicitis, fever was always present; the pain was definitely localized in the right lower quadrant of the abdomen; vomiting was present, but usually not so persistent as in the cases of ketosis, and tenderness and rigidity in the right lower quadrant were present.

Medical management consisted in the subcutaneous administration of 10 per cent dextrose in physiologic solution of sodium chloride in order to restore and maintain the water balance, supply dextrose and restore the depleted chlorides. Insulin was administered at six hour intervals. Urinalyses for dextrose and diacetic acid were made before each dose of insulin.

In this relatively small series of cases acute appendicitis could be differentiated from diabetic ketosis with abdominal pain mainly by localized pain, rigidity and tenderness and moderate fever.

FURTHER STUDIES IN INFANT NUTRITION: RICKETS. DR. JESSE R. GERSTLEY.

Some years ago my associates and I demonstrated that the addition of certain amounts of lactose to the milk formula of an infant led to feces of an acidity and bacteriology nearer those of the breast fed infant than did the addition of dextrin-containing carbohydrates. The stool of the normal breast fed infant is highly acid. At about the same time Bergeim, in experiments on animals, concluded that the intestinal acidity resulting from feeding lactose led to better physiologic usage of calcium and phosphorus than when other carbohydrates were used.

In the present study the effects of feedings of lactose and of dextrin-containing carbohydrates on the development of rickets in infants were compared. Twenty babies were studied for six months, each over a period of four years, the investigation including monthly physical and roentgenologic examination and chemical examination of the blood. The babies who were fed lactose showed a slight clinical superiority. Of equal interest was the suggestion that the caloric content and the proportions of the diet may play a rôle in the etiology of the condition; that much cod liver oil is used unnecessarily (many of the babies receiving cod liver oil showed no clinical or laboratory signs of rickets), and that in establishing the diagnosis of rickets clinical findings prove more sensitive than do physical examination and determinations of blood calcium and phosphorus.

DISCUSSION

DR. CLIFFORD G. GRULEE: There are a few points to which I think that attention should be called. In the first place, like Dr. Gerstley, I have never been able to become unduly excited about rickets. I think that the condition is grossly exaggerated from the pediatric standpoint.

In the second place, it has been known for a long time that marked rickets does not develop in children who are not rapidly growing. I think that it was Jundell who called attention to the fact that a certain amount of overnourishment is necessary for the development of rickets. I wish to point out that institutionalization may be responsible for the fact that these babies do not gain as fast as others. What institutionalization does I do not know, but it affects the nutrition of the child.

The paper shows a great deal of work and of careful thought. There are no conclusions, because there is none to be drawn. The series of cases is too small. But another point that might be made is that obesity in babies is no more to be desired than obesity in adults.

DR. JESSE R. GERSTLEY: I am glad that Dr. Grulee raised the question of hospitalization being a possible factor in determining the weight of these infants. I had this point in my notes but overlooked it in the presentation.

Book Reviews

The Prospective Mother. By J. S. Slemons. Third edition. Price, $2. Pp. 293. New York: D. Appleton-Century Company, 1934.

In this book the reviewer recognizes an old friend, for he has for years recommended it to pregnant women who were desirous of information concerning pregnancy and labor. It has long served a useful purpose in affording simple and easily understandable explanations of the problems of reproduction to women who feel that they may be happier for having an elementary understanding of that important and complicated process which is going on within their own bodies. Too detailed and complicated discussion is avoided, and care has been taken not to print matter concerning the complications of pregnancy and labor which might alarm pregnant women. Additions and changes have been made which bring the book abreast of the times. One may note particularly the inclusion of a brief explanation of the Aschheim-Zondek test and a discussion of the newer methods of anesthesia and analgesia.

In the chapter devoted to the care of the breasts one cannot agree completely with the advice given for "toughening" the nipples. Scrubbing them with a brush seems a drastic and rather painful practice and one not wholly free from the danger of injurious trauma.

The advice given regarding exercise is excellent, and any physician who has reasoned with scores of women about journeys during pregnancy will assent to the views expressed.

The chapter on miscarriage is particularly commended. The subject is discussed in language comprehensible to the woman for whom the book is written. The question of criminal abortion is gone into with a refreshing frankness which would make it difficult for a reader of even limited intelligence to fail to understand that abortion, other than therapeutic abortion done for adequate reasons, is a criminal and immoral act. Such a clear exposition of the matter in a book intended for nonmedical readers will serve a useful purpose in these days of slackening moral standards.

Preparations for labor in the home are discussed, and directions for efficient sterilization with limited facilities are given, but the value of the more efficient surroundings of the maternity hospital is emphasized.

The discussion of the puerperal period, with the clear exposition of the time required for involution, should make it easier for the woman who has read the volume to understand that the apparently conservative advice that she receives from her physician concerning this process is based on physiologic facts.

This book has had a long and useful life. Its success has been deserved, and it has been a source of enlightenment to many prospective mothers. A continuation of this success will, it seems certain, await the third edition.

The Spastic Child. By Marguerite K. Fishel. Price, $1.50. Pp. 97, with photographs and drawings. St. Louis: C. V. Mosby Company, 1934.

This book is written by a parent, who records her personal experience with her two children (who had two different types of Little's disease), together with medical information.

The first child remained so spastic that he was unable to sit up, talk or take care of himself up to 5 years of age, when he died of influenza.

The second child presented a more hopeful picture from the start, and the author portrays the possibility of rehabilitating a certain type of spastic child, even though it first appears to lead the life of a cripple.

The procedure of meeting the subjective and objective problems of the parents is presented so as to be of help in the lives of other parents.

The task is a combined job for the orthopedic surgeon and the physical therapist and is primarily a parent's job. It consists of long labor in adjusting disorganized

muscular control by persistent training in conscious relaxation and conscious muscular movements. This task requires ingenuity and patience over a long period.

As a reward for the effort extended, the mother saw a crippled and socially handicapped child develop as a normal human being.

Der Arzt als Erzieher des Kindes. By Prof. Adalbert Czerny. Eighth edition. Pp. 106. Vienna: Franz Deuticke, 1934.

This is the eighth edition of this booklet composed of seven lectures by Prof. Adalbert Czerny. The chief purpose of the author is to impress on the physician his opportunities and responsibilities as advisor in the rearing of children. The physician is in a unique position as the person to whom the parents turn for advice on problems concerning the management of infants and children. These problems concern every phase of the child's life, and new problems are always arising as the child grows older. In these lectures Czerny draws on his many years of experience as a pediatrician in discussing his impressions and opinions concerning the numerous common questions which a physician is called on to answer concerning the feeding, habits, clothing, play and schooling of children. A wholesome attitude toward behavior problems is especially stressed, as the mental and psychic development, as well as the physical development, of the child is of the utmost importance. This booklet is highly recommended to all physicians dealing with children.

Physical Diagnosis. By Richard C. Cabot. Price, $5. Pp. 540, with 317 illustrations. Baltimore: William Wood & Company, 1934.

This is the eleventh edition of the well known book by Dr. Cabot, emeritus professor of clinical medicine in Harvard University and formerly chief of the west medical service at the Massachusetts General Hospital. The revision is complete, but the characteristic style, method of presentation and profuseness of illustration remain.

Three new chapters on the electrocardiogram, pulmonary heart disease and the heart in myxedema have been added. The section on subacute infectious endocarditis has been rewritten. Recent studies have permitted extensive additions to the chapters on coronary heart disease, tuberculosis, cancer of the bronchi and lungs, pneumonoconiosis and pulmonary embolism. Less extensive changes have been made in several other chapters. The author states: "The section on 'Diagnosis of Pulmonary Emphysema,' on which I hold heretical views, has been enlarged."

The Laboratory Notebook Method in Teaching Physical Diagnosis and Clinical History Recording. By Logan Clendening, M.D. Price, 50 cents. Pp. 71. St. Louis: C. V. Mosby Company, 1934.

The value of this book lies chiefly in the convenience and completeness of its arrangement. One side of the page is blank, except for large headings; on the opposite page are all the points to be noted under different methods of examination of the part in question. Undoubtedly, the use of the book would be valuable in establishing a systematic method of approach to the taking of histories and physical examination, but it seems a bit like spoon-feeding.

Orthopaedic Surgery. By Walter Mercer. Price, temporarily, $8; published, $10.50. Pp. 695, with 371 illustrations. Baltimore: William Wood & Company, 1933.

The field of orthopedic surgery is treated in a thorough manner, however short and concise. Each subject is considered from the standpoint of etiology, pathology, symptoms, diagnosis, differential diagnosis and treatment. This is an excellent work for the student or general practitioner.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.
Place: Bâle, Switzerland: Time: September 1935.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.
Place: Newcastle, County Down, Ireland. Time: May 3-4, 1935.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. R. C. Jewesbury, 5, Wimpole St., London, W. 1.
Secretary: Dr. Helen Mackay, 28, John St., London, W. C. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4: 30 p. m.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. A. Graeme Mitchell, Children's Hospital, Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Atlantic City, N. J. Time: June 10-14, 1935.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New York. Time: June 7-8, 1935.
Region I. Place: Philadelphia. Time: Oct. 11-12, 1935.
Regions II and III. Place: St. Louis. Time: Fall, 1935.
Region IV. Place: Seattle. Time: Fall, 1935.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Borden S. Veeder, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Wade Park Manor, Cleveland. Time: May 2-4, 1935.

Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Buffalo, N. Y. Time: June 1935.

Society for Pediatric Research

President: Dr. Joseph Stokes Jr., Children's Hospital, Philadelphia.
Secretary: Dr. A. A. Weech, Babies Hospital, New York.
Place: Atlantic City, N. J. Time: May 1935.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Armin Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, 1227 Medical and Dental Bldg., Seattle.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Oliver W. Hill, 301 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Charles Abbott, 1817 Broad St., Tuscaloosa.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.
Place: Mobile. Time: April 17-19, 1935.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Benjamin Bashinski, 700 Spring St., Macon.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Lonis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Matthew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. John Signorelli, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Edwin A. Socola, 1027 Canal Bank Bldg., New Orleans.
Place: New Orleans. Time: April 29, 1935.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George Sincerbeaux, 6 William St., Auburn.
Secretary: Dr. John D. Craig, 12 E. 11th St., New York.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. C. V. Rice, 222 Wall St., Muskogee.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Place: Oklahoma City. Time: May 1935.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.
Place: Harrisburg. Time: Sept. 30-Oct. 3, 1935.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Arthur G. Jacobs, 1193 Madison Ave., Memphis.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Nashville. Time: April 1935.

TEXAS PEDIATRIC SOCIETY

President: Dr. Ramsay H. Moore, 3600 Fairmount St., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. P. McDowell, 142 W. York St., Norfolk.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of each month from October to May, 8:30 p. m.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. C. V. Mulligan, 17 Walmer Rd., N., Toronto.
Secretary: Dr. T. B. Verner, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Stanley Gibson, 9503 Prospect Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: John B. Murphy Memorial Bldg. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Earl W. May, 1551 Woodward Ave., Detroit.
Secretary: Dr. E. A. Wishropp, 10 Peterboro Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little Jr., 817 Holman Ave., Houston, Texas.
Place: Houston Club: Time: Third Monday of each month.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y.: Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwuakee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Harry Bakwin, 132 E. 71st St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. O. W. Rowe, 205 W. 2nd St., Duluth, Minn.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Place: Minneapolis. Time: Spring, 1935.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Carl K. Wagener, Jenkins Arcade, Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklln St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

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